SEVENTH FRAMEWORK PROGRAMME
THEME [3]
[Information and Communication Technologies]

Grant agreement for: **Large-scale integrating project**

Annex I - "Description of Work"

Project acronym: ***Epiwork***
Project full title: **Developing the framework for an epidemic forecast infrastructure**

Grant agreement no.: *231807*

Date of preparation of Annex I (latest version): October 8, 2008.

Date of approval of Annex I by Commission: *13 October 2008*

List of Beneficiaries

Beneficiary Number *	Beneficiary name	Beneficiary short name	Country	Date enter project	Date exit project
1(coordinator)	Fondazione Istituto per l'Interscambio Scientifico	ISI	Italy	1	48
2	Fundação Calouste Gulbenkian	FGC-IGC	Portugal	1	48
3	Tel Aviv University	TAU	Israel	1	48
4	Max Planck Gesellschaft zur Foerderung der Wissenschaften E.V.	MPG	Germany	1	48
5	Acquisto Inter BV	AIBV	The Netherlands	1	48
6	London School of Hygiene and Topical Medicine	LSHTM	United Kingdom	1	48
7	SMITTSKYDDS Institutet	SMI	Sweden	1	48
8	Katholieke Universiteit Leuven	KULeuven	Belgium	1	48
9	Bar Ilan University	BIU	Israel	1	48
10	Fondazione Bruno Kessler	FBK	Italy	1	48
11	Center for REsearch And Telecommunication Experimentation for NETworked communities	CREATE-NET	Italy	1	48

12	Faculty of Sciences University of Lisbon	FFCUL	Portugal	1	48

Table of contents

Part A

A.1 Overall budget breakdown for the project

Eligible costs and requested contribution

Particip ant	RTD / Innovation (A)	Demons tration (B)	Management (C)	Other (D)	Total (A+B+C+D)	Total receipts	Requested EC contribution
ISI	585,600.00	0.00	224,000.00	104,771.00	914,371.00	0.00	767,971.00
FCG-IGC	646,400.00	0.00	6,800.00	0.00	653,200.00	0.00	491,600.00
TAU	528,000.00	0.00	4,000.00	0.00	532,000.00	0.00	400,000.00
MPG	531,333.00	0.00	3,000.00	0.00	534,333.00	0.00	401,499.00
AIBV	687,000.00	0.00	60,800.00	0.00	747,800.00	0.00	576,050.00
LSHTM	469,500.00	0.00	0.00	0.00	469,500.00	0.00	352,125.00
SMI	529,568.00	0.00	2,800.00	0.00	532,368.00	0.00	399,976.00
K.U.Leu ven	266,667.00	0.00	0.00	0.00	266,667.00	0.00	200,000.00
BIU	373,332.00	0.00	3,000.00	0.00	376,332.00	0.00	282,999.00
FBK	323,600.00	0.00	0.00	0.00	323,600.00	0.00	242,700.00
CREATE-NET	293,120.00	0.00	0.00	16,640.00	309,760.00	0.00	236,480.00
FFCUL	660,800.00	0.00	3,000.00	0.00	663,800.00	0.00	498,600.00
Total	5,894,920.00	0.00	307,400.00	121,411.00	6,323,731.0	0.00	4,850,000.00

A.2 Project summary

In recent years a huge flow of quantitative social, demographic and behavioural data is becoming available spurring the quest for innovative technologies that can improve the traditional disease-surveillance systems, providing faster and better localized detection capabilities and resulting in a broad practical impact. Improved ICT techniques and methodologies support the inter-linkage and integration of datasets causing a qualitative change in the ways we can model epidemic processes. Visualization and analysis tools able to cope with multiple levels of representation are being developed along with computer simulations that provide experiments not feasible in the real world. For the first time, ICT and computation enable the study of epidemic in a comprehensive fashion that addresses the complexity inherent to the biological, social and behavioural aspects of health related problems. The EPIWORK project proposes a multidisciplinary research effort aimed at developing the approriate framework of tools and knowledge needed for the design of epidemic forecast infrastructures. The research considers most of the much needed development of modeling, computational and ICT tools such as i) the foundation and development of the mathematical and computational methods needed to achieve prediction and predictability of disease spreading in complex social systems; ii) the development of large scale, data driven computational models endowed with a high level of realism and aimed at epidemic scenario forecast; iii) the design and implemention of original data-collection schemes motivated by identified modelling needs, such as the collection of real-time disease incidence, through innovative web and ICT applications. v) the set up of a computational platform for epidemic research and data sharing that will generate important synergies between research communities and countries.

A.3 List of beneficiaries

Beneficiary Number *	Beneficiary name	Beneficiary short name	Country
1(coordinator)	Fondazione Istituto per l'Interscambio Scientifico	ISI	Italy
2	Fundação Calouste Gulbenkian	FGC-IGC	Portugal
3	Tel Aviv University	TAU	Israel
4	Max Planck Gesellschaft zur Foerderung der Wissenschaften E.V.	MPG	Germany
5	Acquisto Inter BV	AIBV	The Netherlands
6	London School of Hygiene and Topical Medicine	LSHTM	United Kingdom
7	SMITTSKYDDS Institutet	SMI	Sweden
8	Katholieke Universiteit Leuven	KULeuven	Belgium
9	Bar Ilan University	BIU	Israel
10	Fondazione Bruno Kessler	FBK	Italy
11	Center for REsearch And	CREATE-NET	Italy

	Telecommunication Experimentation for NETworked communities		
12	Faculty of Sciences University of Lisbon	FFCUL	Portugal

Part B

B1. Concept and objectives, progress beyond state-of-the-art, S/T methodology and work plan

B.1.1 Concept and project objectives

- ***Background***

The current threats of pandemic influenza, HIV and XDR tuberculosis, and recent threats such as SARS and the release of bioterrorist agents, raise major urgent concerns with regard to public health preparedness, risk management and decision making (WHO-EPR; Jones et al., 2008; Morens et al., 2004; Smolinski et al., 2003; Binder et al., 1999; Daszak et al., 2000; Taylor et al., 2001; Patz et al., 2004; Weiss et al., 2004; Woolhouse and Gowtage-Sequeria, 2005; Morse, 1993; King et al., 2006). Mathematical models have become important tools in analyzing the spread and control of these threats and assist decision makers in taking proper prevention and containment/mitigation measures (Anderson and May, 1991; Dieckmann and Heesterbeek, 2000; Daley and Gani, 1999; Keeling and Rohani, 2008, Riley, 2007). Recent years have seen an increasing trend in the number of publications in the epidemiological literature, both in all journals and high impact journals, that use mathematical models (Keeling and Rohani, 2008). They are now "as crucial in the study of infectious diseases as are microscopes, stethoscopes, and the tools of molecular diagnosis" (Dobson, 2008). They are used in assessing the impact of infectious disease epidemics and pandemics to human health (Riley, 2007; Longini et al., 2005; Ferguson et al., 2005, Ferguson et al., 2006; Hufnagel et al., 2004; Colizza et al., 2007a, 2007b; Cooper et al., 2006; Germann et al., 2006; Halloran et al, 2002, Pitman et al., 2005, Ferguson et al., 2003; Camitz and Liljeros, 2006; Ciofi degli Atti et al., 2008; Ajelli and Merler, 2008). Their role in comparing, planning, implementing and evaluating various control programs, is of major importance for public health decision makers.

Recent years have also witnessed a tremendous progress in data gathering, development of new informatics tools, and increase in computational power. All these aspects have a crucial impact on our ability to accurately model infectious diseases. The spread of epidemics is indeed inevitably entangled with human behavior, social contacts, and population mobility and mixing. A huge flow of quantitative social, demographic and behavioural data is becoming available, that trace the activities and interactions of individuals, social patterns, transportation infrastructures and travel fluxes (Barrett et al., 2000; Liljeros et al., 2001; Chowell et al., 2003; Schneeberger et al., 2004; Barrat et al., 2004; Guimera et al., 2005; Brockmann et al., 2006; Onnela et al., 2007, Mossong et al., 2008; de Blasio et al., 2007). Improved techniques and methodologies support the inter-linkage and integration of datasets with geo-referenced information and economical and transportation databases (BTS, GIS). This has caused a qualitative change in the ways we model epidemic contagion processes. Visualization and analysis tools able to cope with multiple levels of representation are being developed along with computer simulations that provide experiments not feasible in the real world (Eubank et al., 2004). A quest for innovative technologies comes also from the disease outbreak detection point of view. Innovative technologies can improve the traditional disease-surveillance systems (EISS), providing faster and better localized detection capabilities and resulting in a broad practical impact (Influenzanet, Marquet et al., 2006; van Noort et al. 2007). *For the first time, epidemic processes can be studied in a comprehensive fashion in a manner that addresses the complexity inherent to the biological, social and behavioural aspects of health related problems. In other words we are in the position to envision the development of large data and computational forecast infrastructures aimed at the realistic prediction, and containment, of the diffusion and impact of infectious disease.*

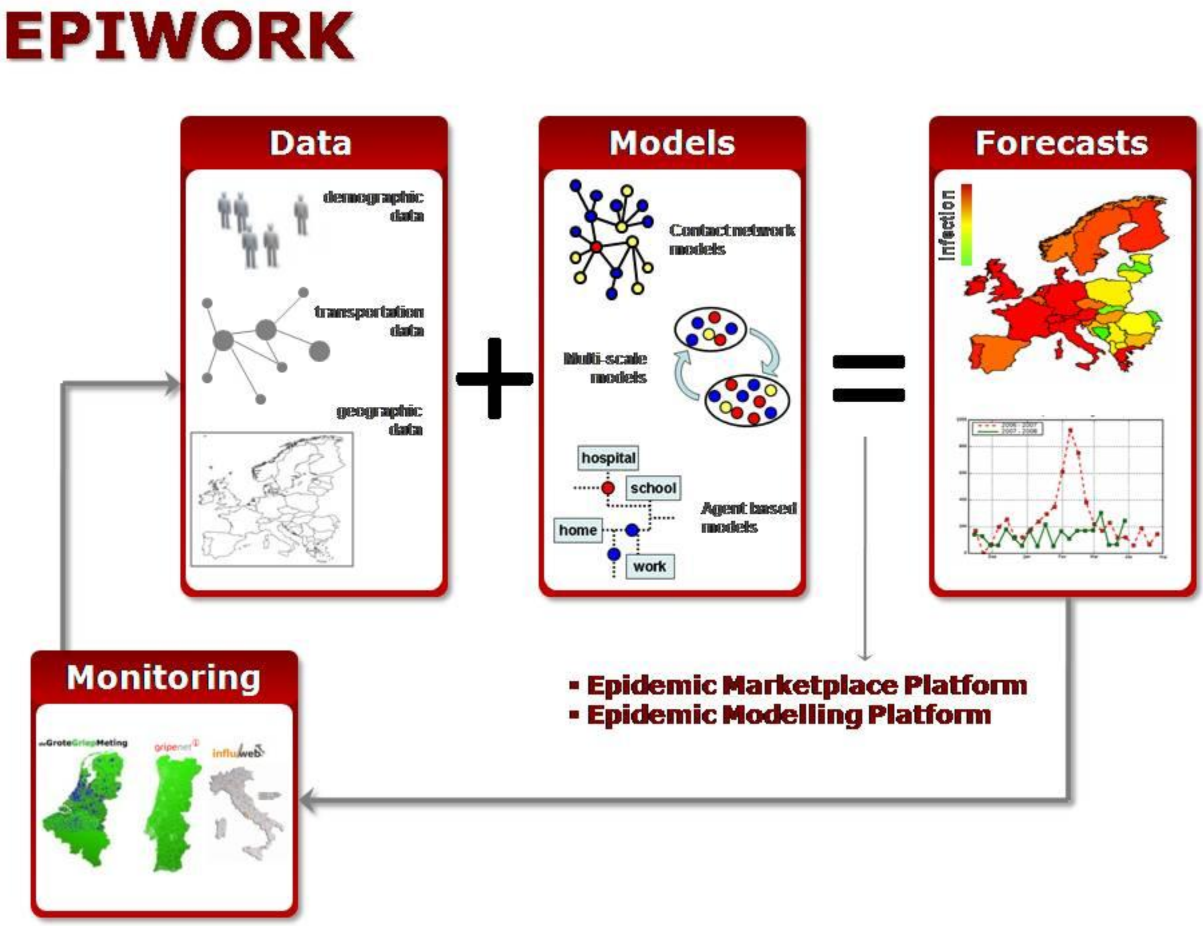

Diagram 1: Schematic representation of EPIWORK project.
The diagram highlights the main components of EPIWORK and their integration to reach the overall aim of the project.

However, it has become clear that any new and significant scientific progress in epidemic research requires a novel interdisciplinary integration of expertise, techniques, and methodologies that interfaces computational and data-intensive science with mathematical epidemiology and an innovative use of Information and Communication Technologies (ICT) to gain knowledge on human, social and economical systems. Indeed, the development of *predictive tools* based on *data driven modelling* requires a combined research effort integrating and assimilating a vast range of mathematical, statistical and informatics expertise and ultimately requires a flexible large-scale interface with high quality surveillance systems at the European and global scale. While the EC has supported research networks dedicated to the development of mathematical, computational and statistical models for infectious diseases and databases construction (MODELREL, INFTRANS, POLYMOD, IRIDE, EUPHIN), in most of the cases the modelling and databases projects proceeded in parallel tracks, targeting different needs and communities. MODELREL aims to establish a robust, consensual and co-ordinated EU capability in modelling to help counter deliberate releases of biological agents, and other potential larger impact natural epidemics. INFTRANS (Infectious Disease: Modelling for Control) plans to establish a warehouse of spatial demographic and population movement data for modeling infectious disease spread in the EU and develop new tools for real-time prediction of infectious disease outbreaks. POLYMOD overarching goal is to strengthen public health decision making by developing and applying mathematical, economic and risk assessment models of infectious diseases. The EC has also supported the development of databases for infectious diseases, such as IRIDE that started in 1997

as an Inventory of resources and means for controlling communicable diseases in the EU and the EUPHIN databases targeted to community, member states and professionals as users. All these project however take into consideration only one aspect of the problem without creating the feedback loop among data-modeling-monitoring efforts. In addition, the complex systems features of epidemiological systems are not addressed in any of these systems as well as no one of those exploits ICT and computational thinking in a forecasting perspective.

Indeed, the vision of a working epidemic forecast infrastructure does require an integrated approach to data, modelling and surveillance that builds on the results of previous projects and systematically redesigns the collaborative interaction among the stakeholders of the various activities. Most important, the modelling frameworks need to be enlarged in order to deal with the complex features of present techno-social systems. These systems are characterized by large sizes (thousands to millions of elements), irregular and scale-dependent structure, time dependence and emergent phenomena and patterns (Albert and Barabasi, 2000; Dorogovtsev and Mendes, 2003; Pastor-Satorras and Vespignani, 2003). The challenge is therefore to determine the long range, long term behaviour of the epidemic which cannot be trivially inferred from the short range interactions included in the models. This implies the use and development of techniques dealing with complex systems features as well as developing new models and mathematical tools able to attain quantitative predictability in large scale techno-social systems. As in weather forecasting, a large scale epidemic forecast infrastructure needs to rely on sophisticated computational tools to integrate present data and huge libraries of previous epidemic patterns into realistic modelling framework. Data gathering has to be informed on the modelling needs as models have to be refined according to the accessible data. Real time data acquisition and sharing should be considered as a key concept as it is in weather predictions; nobody would think to predict weather on the basis of the meteorological situation of two months ago. Data and algorithm sharing to the community at large, still in real time, is an essential requirement. Finally the development of appropriate user interface that would make modelling power available to researchers outside the close circle of mathematical and theoretical epidemiologists is necessary to make an epidemic forecast infrastructure a concrete and useful tool for policy makers and health institutions. This can be ultimately done only by the opportune use of modern ICT technologies.

- ***Work Areas***

Building on a multidisciplinary research approach, the projects aims at developing the approriate framework of tools and knowledge needed for the design of epidemic forecast infrastructures. It is based on a highly synergistic, interdisciplinary effort among computational modellers, medical scientists, epidemiologists, and computer scientists. The project aims at exploring the following *work areas* as the major research themes directly matching the objectives of this proposal and representing the necessary steps toward the future construction of an epidemic forecast infrastructure:

- **Modelling and theoretical foundations.** The research effort ranges from the analysis of stylized models (Anderson and May, 1991; Dieckmann and Heesterbeek, 2000; Daley and Gani, 1999; Stone et al., 2007; Keeling and Rohani, 2008; Gomes et al. 2002, 2004a, 2004b, 2005; Águas et al. 2006, 2008; Lopez et al., 2007; Gallos et al., 2007; Madar et al., 2007; Ajelli et al., 2008; Stollenwerk et al., 2007, Massad et al., 2008) that can provide basic insights in the epidemiological theory to computational approaches for large scale (spatially extended) simulations aimed at realistic scenario analysis (Riley, 2007). The latter are used as in silico epidemic experiments that, including the detailed complexity of real-world population mobility and host-pathogen interactions, allow researchers to assess the epidemic evolution and to test interventions to mitigate its impact on the population (Stone et al. 2000; Cohen et al., 2003; Riley, 2007; Longini et al., 2005; Ferguson et al., 2005, Ferguson et al., 2006; Hufnagel et al., 2004; Colizza et al., 2007a, 2007b; Cooper et al., 2006; Germann et al., 2006; Halloran et al, 2002; Eubank et al., 2004, Pitman et al., 2005; Ferguson et al.,

2003, Camitz and Liljeros, 2006, Ciofi degli Atti et al., 2008; Ajelli and Merler, 2008). The integration of detailed data of techno-social systems requires basic theoretical and algorithmic foundations for the understanding of the fundamental principles and mechanisms that govern epidemic behaviour in *large scale complex multi-scale network and individual based epidemic models*. In this area a crucial point is the understanding of the impact of large scale *complex features* (scale invariance, extreme heterogeneity, large-scale fluctuations) of interaction and communication networks on epidemic spreading patterns (Pastor-Satorras and Vespignani, 2001; Lloyd and May, 2001; Eames & Keeling 2002; Barthelemy et al., 2005; Colizza et al., 2006; Eames 2008; Lopez et al., 2007; Gallos et al., 2007; Madar et al., 2007).

- **Data-driven computational platform.** Given the complexity and increasingly interconnectedness of our world, with no closed boundaries between countries, any epidemic forecast effort is crucially dependent on the accessibility to transnational demographic and mobility data, uniform standards to collect detailed spatio-temporal disease incidence, immunization and pathogen evolution data. Such a *data integration* and assimilation capacity requires the design, implementation, and demonstration of a *computational platform for epidemic research and data sharing.* The platform will allow detailed, accurate and reliable simulations for real time and predictive modelling of epidemic events, available to researchers, health-care professionals and policy makers.
- **ICT monitoring and reporting system.** A novel monitoring infrastructure would provide crucial advantage to modellers for real-time data feed to forecast algorithms. This Work Area has the ambition to generalize and evolve the system developed in the Netherlands and in Portugal for the *web collaborative monitoring* of disease incidence (Influenzanet). This system is conceived to inform and educate the population about the disease and to collect real-time information on population health through web-services. Graphic representation, processing and analysis of data on the progression of the disease, is provided in real time. Population-based real-time monitoring, under development in Sweden, promises further refinement of patient-initiated disease reporting using state-of-the-art telecommunication and Internet techniques, guaranteeing the link to the underlying population that generates the cases. Standardized methods would allow monitoring the evolution of an epidemic across country boundaries in a consistent way, with real time alerts to rapidly identify public health emergencies, and estimate key epidemiological parameters to devise and test methods to contain them.

The work areas targeted in this paper need to be developed in the presence of a mutual feedback and strong collaborative approach among the researchers involved in the project, fostering crucial flows of information and knowledge production in the data-modelling-application process. This level of integration is possible only within a large integrated project providing a framework and shared vision for the overarching goals of the project.

- ***Objectives***

A fully operational, accurate and reliable epidemic forecast infrastructure nowadays faces problems related to the lack of appropriate models to understand how an infectious disease spreads in the real world, lack of extensive and accurate epidemiologically relevant data (from societal data to epidemic surveillance data), lack of understanding of the interplay among the various scales of the problem (from the host-pathogen interaction, to human-to-human transmission, to the interaction with the environment) and most importantly lack of communication among the different areas of research which proceed almost independently, crucially hampering a significant progress in a highly interdisciplinary field of research. The present project intends to fill this gap. *Through computational thinking, complex systems concepts and data integration tools relevant for epidemiological understanding at all levels, it will provide a set of radical, paradigm-changing results enabling a novel approach to the modelling, forecast and policy making approach to infectious diseases.* The projects overarching goals are:

- The identification of general principles and laws that characterize complexity and capture the essence of *complex epidemiological systems*.
- The development of a *collaborative information platform* enabling the production of knowledge, understanding and models from the novel *abundance of digital data in epidemic research*.
- The development of an *open, data driven, computational modelling platform* to be used in epidemic research as well as in policy making for the analysis of global epidemics, integrating and leveraging on transnational data.
- The development, deployment and validation of an *Internet-based Monitoring System (IMS) producing real time data on disease incidence and epidemic spreading*.

- ***Methodology***

We address the above issues with the intention to initiate a community approach to the problem and develop an armoury of tools and knowledge that will produce a quantum leap in the state of the art of epidemic research. The project involves a number of different groups that represents the whole spectrum of disciplines needed for a fruitful and truly interdisciplinary approach to the problem. The team includes computer scientists and physicists experts in data analysis and integration, and computational modelling. Three groups of mathematical epidemiologists lead the basic modelling definition and constructions. Three groups of epidemiologists representing centres for disease control in the respective countries supervise the data analysis and acquisition and work on validating the results and tools developed in the project. One consultancy and project management firm supervises the deployment of the proposed Internet-based monitoring system on a global European scale.

While our project might sound very ambitious, it revolves around a clear set of tasks that will lead to substantial improvements in the data gathering and integration processes and will allow the development of new classes of realistic *epidemic models able to cope with the complex realities of techno-social systems*. The research considers most of the much needed development of modelling, computational and ICT tools in epidemic research such as the foundation and development of the mathematical and computational methods needed to achieve *prediction and predictability* of disease spreading in *complex social systems*. Furthermore, the development of large scale, data driven *computational models* endowed with a high level of realism, the design and implementation of *original data-collection schemes* including real-time disease incidence data and the set up of a *computational platform for epidemic research and data sharing* will generate crucial synergies between research communities and countries, fostering a collective approach to the prevention, detection, and timely response to any public health emergency of national and international concern.

B.1.2 Progress beyond the state-of-the-art

Infectious diseases remain a serious medical burden all around the world with 15 million deaths per year estimated to be directly related to infectious diseases (Morens et al., 2004). The emergence of new diseases such as HIV/AIDS, the severe acute respiratory syndrome (SARS) and the eventual rise of a new influenza pandemic represent a few examples of the serious problems that the public health and medical science research need to address (Jones et al., 2008; Morens et al., 2004; Smolinski et al., 2003; Binder et al., 1999; Daszak et al., 2000; Taylor et al., 2001; Patz et al., 2004; Weiss et al., 2004; Woolhouse and Gowtage-Sequeria, 2005; Morse, 1993; King et al., 2006). While for centuries, mankind seemed helpless against these

sudden epidemics, in recent time our ability to control future epidemic outbreaks is to a high degree facilitated by the advances in modern science (King et al., 2006). The cures for a number of dangerous pathogens are available and thanks to the genetic revolution new drugs to prevent and reduce the health consequences of new epidemics can be developed and manufactured faster with respect to the past. On the global scale, the World Health Organization and other agencies have put in place cooperative infrastructures for disease control and surveillance that allow a timely identification and track of emergent disease evolution and spread, enabling the alert of national and international health services and the deployment of containment measures (WHO-EPR). On the other hand, however, the increasing population of urban areas, the massive interconnectivity among world regions and the human mobility are factors which accelerate the spread and diffusion of old and new diseases (Dye, 2008; Morens, 1998; Peiris et al., 2003, Patz et al., 2004; Weiss et al., 2004). In this context, diseases and epidemics can have far reaching effects on a very short time scale (WHO-SARS). As a result, we demand ever-increasing predictive power to anticipate future outbreaks and evaluate associate risks. The successful containment of the next pandemic event is not just linked to our medical infrastructure but also on our capacity to predict its diffusive pattern and optimize medical and mitigation policies. In such containment processes, the ability to forecast how a disease might spread on the local and global level (as much accurately as we can now do for the weather) is essential for the identification and development of appropriate control strategies. In this perspective, computational power and ICT advances allow us for the first time to ambitiously imagine the creation of computational epidemic forecast infrastructures able to provide reliable, detailed and quantitatively accurate predictions of global epidemic spread.

To reach this goal, knowledge as well as resources need to be accessed, shared and integrated among researchers working in this area – epidemiologists, computer scientists, mathematical biologists, information scientists, medical scientists. Strong collaboration, shared information and integration of different expertise are the crucial points of this proposal and the key to address a complex problem that involves elements non-trivially interacting with one another at different time and length scales, from virus to host to population to environment. Feedback loops connecting the different areas of research are fundamental in allowing further improvement in a multidisciplinary field of research that otherwise would be hampered by transdisciplinary boundaries. A true progress in knowledge production and understanding the spread of human infectious diseases requires a systematic redesign of the research approach in terms of integration, multidisciplinary effort and collaborative interactions among the stakeholders of the various activities, building on the results and experience reached in previous projects. A realistic and reliable large-scale epidemic forecast infrastructure will involve such a high level of complexity and realism that its progress in parallel non-communicating tracks, targeting different needs and communities is bound to fail. Real data needs to be analyzed to refine and design appropriate modelling approaches, and models require data as input ingredient. Data availability across physical and non-physical boundaries (such as national borders, linguistic barriers, and disciplines boundaries) as well as uniform and standardized approaches are an essential requirement. Availability to the community at large of data, information and computational approaches in epidemic research through an appropriate user interface would make modelling power a concrete and useful tool for assessing scenarios, predicting epidemic evolution, managing health emergencies, benefiting a large audience of users, including researchers, non-experts, policy makers, and health institutions. On the other hand, the above research plan needs the constant inputs and contribution of epidemiologists, mathematical biologists and public health experts. The basic research questions and the practical use and implementation of the predictive power derived by modelling and computational results must be informed and defined with epidemic and health researchers.

The aim of the project is to produce non-incremental advances in the capability of forecasting the spreading of infectious diseases, relying on modelling and computational tools able to provide scenario forecast, risk assessment and containment measure testing contextually to the onset of health crisis as well as for recurrent

and seasonal events. In other words, the capability of statistically predicting incidence, morbidity, mortality spatio-temporal patterns for epidemics and pandemic events and to evaluate medical and non-medical interventions such as drugs deployment, vaccination, social distancing. The present state of the art in the field has serious limitations hindering our forecast capabilities, and the present proposal intends to tackle those limitations both in the modelling, data and experimental areas. For this reason the consortium gather experts in a wide range of disciplines ranging from physics and computer science to theoretical epidemiology and public health. The top rate expertise of the consortium in mathematical epidemiology, epidemiology and public health anchors the project to the actual questions and challenges of the field and provides a truly multidisciplinary approach. In the following we provide a discussion of the advancement beyond the state of the art offered by the present proposal in each of the main Work Areas targeted by the project.

B.1.2.1 Modelling and theoretical foundations.

A first limitation of the state of the art in epidemic modelling and forecast is the large gap between the classical epidemiology theory, dominated by stylized models, and the theoretical understanding of the many complex facets encountered in the realistic description of epidemics. Epidemic models are largely based on random populations or very simplified contact patterns. The multiscale complexity of the population-disease-environment system and the dynamical aspects of contacts and mobility of individuals, as well as other time dependent features such as seasonal effects and other external environmental drivers are generally not included in the model formulation (Stone et al., 2007). Analogously, the complexity added by the interaction between pathogen and host, vaccination procedures, short and long-term immunity, and reinfection mechanisms has been investigated only at the level of very simple compartmental models (Gomes et al., 2002, 2004a, 2004b, 2005; Aguas et al., 2006; Stollenwerk et al., 2007). The mathematical epidemiologists and modellers in the consortium intend to finally lay the foundation of new models stylized enough as to remain analytically tractable, yet nevertheless accurate to simulate realistic heterogeneous epidemic processes. In the case of complex systems, this task amount to distinguish different classes of parameters and to identify which ones are really relevant in the description of the behaviour of the system, obtaining models which stay at a reasonable level of precision but still captures enough realism in order to be useful in practical situations.

Complexity of the population-disease-environment system

The work carried out during the project will define models considering that the contact patterns among individuals over which the disease spreads are highly heterogeneous, leading to the emergence of high -risk individuals and potential super-spreaders, and thus making the variations in people's interacting behaviour a crucial determinant of individual-level risk (Eames and Keeling 2002; Cohen, Havlin, BenHavram 2003, Eames 2008; Mossong et al, 2008; de Blasio et al., 2007). This will determine how heterogeneities due to population aggregations and spatial structuring control the epidemic size and the extinction threshold as well as competition and evolution between disease strains. The project will also focus on the interplay between seasonality and pathogen competition and evolution and their complex effects in epidemic evolution (Stone et al. 2007). These results allow a new take on the design of vaccination intervention and the effect of reinfection thresholds and pathogen dynamics (Gomes et al., 2002, 2004a, 2004b, 2005; Aguas et al., 2006; Stollenwerk et al., 2007). The proposed work is therefore providing major theoretical and algorithmic advances in crucial areas such as

- Characterization of heterogeneities due to population aggregations and spatial structuring.
- The impact of seasonality and other external environmental drivers in techno-social systems of epidemic relevance.
- New vaccination and containment strategies that exploit the complex properties of the systems: for instance the targeting of appropriate hubs in populations with heavy-tailed connectivity patterns.

- The effect of temporal correlations and evolution (reinfections, immunity, antigenic variations) at the population level.

These results and the new model structures will change parameter estimation schemes and the project will develop new tools for estimating key parameters on real data and evaluate the prediction quality of the models. By combining the different theoretical developments and parameter estimation methods the Consortium epidemiologists expect to make significant advances to the understanding of what components must be included in early warning systems for infectious diseases.

The structure of interacting populations on many magnitude and spatial scales

Another shortcoming of the present state of the art in epidemic modelling is represented by the lack of understanding and characterization of the complex structure of metapopulation models. Large scale models of epidemic evolution in fact crucially dependent on the ability to quantify the topological and dynamical features of human mobility network and spatially structured models (the basic brick of epidemic forecast computational approaches) (Riley, 2007; Longini et al., 2005; Ferguson et al., 2005, Ferguson et al., 2006; Hufnagel et al., 2004; Colizza et al., 2007a, 2007b; Cooper et al., 2006; Germann et al., 2006; Eubank et al., 2004, Pitman et al., 2005; Camitz and Liljeros, 2006, Ciofi degli Atti et al., 2008; Ajelli and Merler, 2008). This in turn requires the development of theoretical frameworks providing order parameters, the identification and extraction of universal features and the quantification of differences and similarities on an international, national and regional level. Despite considerable effort and advances in the study of human transportation networks, e.g. investigations of statistical properties of specific human transportation networks (Barrat et al., 2004; Guimera et al., 2005), no systematic investigation of traffic networks incorporating all spatial scales exists today. As such our understanding of human mobility within heterogeneous and spatially structured populations is limited. The project envisions overcoming two of the most challenging aspects of complexity in this context, namely, the structure of interacting populations on many magnitude and spatial scales beyond and within international, interregional, intercultural and linguistic boundaries and their effective interaction by means of multi-length scale transportation and mobility networks. The project will combine the analysis of extensive transnational transportation dataset with new sources of pervasive online data such as i) Eurobilltracker.com that investigates the dispersal of individual bank notes registered at the online bill tracking system; ii) Geocaching.com, a modern, international GPS treasure hunt in which trackable items are transported by travelling humans from place to place and iii) bookcrossing.com an internet administered game of similar nature. These data sets provide an unprecedented amount of information on particular aspects of human mobility with very high spatio-temporal accuracy and across international boundaries and will define a class of proxy mobility networks that complementing regular transportation data will to provide a global multiscale picture of human dynamics. The proposed research will provide a first principles construction of the meta-population description that goes beyond the usual identifiable structured contexts such as cities, town and villages, or – on a smaller scale – schools, workplaces and homes. The complexity of the techno-social systems makes these intuitive modules opaque or arbitrary and the project will work on defining novel community structure identification algorithms to identify the effective community structure in multi-scale mobility networks.

Network-network duality framework

The combination of the results on contact patterns among individuals (Mossong et al., 2008) and the metapopulation structure represents another major conceptual and theoretical advance proposed by the project: the understanding of human interactions in a network-network duality ansatz. The statistical properties of contact networks are strongly influenced by the way individuals behave as agents in a spatially structured meta-population. Contemporary research on disease dynamics has so far not succeeded in merging these two aspects. We anticipate bridging this gap in a network-network duality framework. The key result is the understanding of the reciprocal impact of social networks and mobility networks. To what extent are contact networks determined by mobility networks and vice-versa? In this approach we plan to develop

mathematical tools and theoretical frameworks that allow the development of models in which social contact networks and mobility networks are modelled simultaneously.

B.1.2.2 Data-driven computational platform.

Modelling platform

The computational approach to the realistic modelling of infectious diseases is at the moment a research area witnessing a few competing groups developing computational models tailored for specific world regions or systems, which require specific expertise and are not accessible to researchers outside the circle of experts in the field. This often implies re-inventing the wheel and the duplication of computational efforts. In addition, these modelling approaches are not critically examined and their actual predictive power is rarely assessed. The research agenda of Epiwork has a twofold approach to overcome these problems:

- The collaboration of epidemiologists, computational modellers and physicists will allow tackling foundational issues related to complexity and predictability in computational epidemiology.
- The development and implementation of a modelling platform available through the web to a wide range of users to simulate epidemics by explicitly including the complexity of the real world.

On the foundational issues, the envisioned work will provide a basic understanding of the predictive time scale as a function of information available on the system and its initial conditions. While the analysis of chaotic properties in basic epidemic models has a long tradition, computational epidemiology faces issues related to the large scale of the extended dynamical systems and its complex properties for the first time. The project will leverage on the collaboration of epidemiologists, physicists and modellers. This will allow the assessment of issues concerning the complexity and predictability of epidemic spreading patterns resulting from multi-scale and agent based computational models by integrating techniques used in information theory and statistical physics (Zurek, 1990; Badii and Politi, 1999; Kinchin, 1957) while at the same time considering the relevant epidemiological parameters, the plausible uncertainties and data bias. The modelling platform will integrate models, real-data and visualization techniques to perform simulations and provide access to the state-of-the-art computational modelling to a wide audience of both experts and non-experts. In particular, transportation data on the mobility of the individuals need to be integrated in epidemic models as the human mobility is the key factor in interpopulation disease spreading. We plan to include data on the commuting of individuals and long range travelling fluxes (airliners, railways) in order to define coupling fluxes among subpopulations in different geographical areas. These fluxes will determine the number of disease carrying individuals that will spread the disease both in agent based models and stochastic metapopulation models. Indeed, the transportation and mobility pattern is nowadays what determines the spatio-temporal pattern of disease on the large scale, entangling the population and infrastructure networks of our societies in creating the spreading substrate of modern diseases.

The final aim is to provide a flexible and user-friendly tool for the simulation of a case study, test and validation of specific assumption on the spread of a disease, understanding of observed epidemic patterns, study of the effectiveness and results of different intervention strategies, analysis of risk through model scenarios, forecasts of newly emerging infectious diseases. The platform will be informed and tested by the consortium epidemiologists and public health professionals and is also envisioned as scenario and training tool for public health workers and policy makers, fostering the use of computational and informatics approach beyond the circle of simulations experts. This platform will work on the open source agreement and is supposed to seed a European effort in the computational modelling of infectious diseases at the moment limited to a very few research groups working independently. The consortium has expert working in protection agencies and ongoing collaboration with the crisis room and pandemic exercises across Europe and we will leverage of these activities to propose our computational platform as a predictive or scenario drawing tool in these contexts. This will allow the exploitation of research synergies and the eventual

nucleation of a large scale computational infrastructure for epidemic modelling in realistic complex techno-social systems. This is the basic component along with the data integration/sharing platform toward the construction of a large scale European epidemic forecast infrastructure.

Information platform

Another limiting factor toward realistic epidemic forecast is the difficulty in assimilating and integrating the ever increasing wealth of datasets needed to support the modelling approach and to extract knowledge and pattern from multiple data source. As of today, data are generally gathered according to different standards and usually collected by national census bureau, health institutes and centres for disease control without coordination. The situation is even more cumbersome for scientific experiment or targeted epidemiological data acquisition. The project envisions a unified and integrated approach for the management of these resources, with the design and implementation of an Epidemic Marketplace Platform, publicly available on the web. The project will define a simple reference format which will facilitate the navigation and use of the datasets. This information platform will provide the community with an unprecedented tool in the epidemic research field with the following enabling features:

- It will support the sharing and management of epidemic datasets and resources as well as their rating, annotation, and selection.
- It will be used as an on-line social networking site that will serve researchers, practitioners, and educators all over the world to foster a virtual community for epidemic research.
- It will support the exchange of resources as well as user interactions. Based on some of the Web2.0 characteristics, users will become active participants, generating information and providing data for sharing, and collaborating online, rather than being satisfied with a passive information consumer/viewer role.
- It will create an exchange point connecting modellers who search for data for deriving their models and those who have data and search for the help of modellers on interpreting their data.
- As collaborations evolve, through direct trustful sharing of data, the platform will also serve as a forum for discussion and the organisation of meetings that will guide the community into uncovering the necessities of sharing data between providers and modellers.

The project has chosen to implement the system on a grid platform (Foster, 2002) based on standards defined by the Open Grid Forum (OGF, 2008), the Globus Alliance (Globus, 2008, Foster 2005) and the OASIS consortium (OASIS, 2008). We intend also to integrate the infrastructure deployed for this project with European grid initiatives such as EGEE (EGEE, 2008). Grid computing (Foster, 2002) aims at the provision of a global ICT infrastructure that enables a coordinated, flexible, and secure sharing of diverse resources, including computers, applications, data, storage, and networks across dynamic and geographically dispersed organizations and communities (sometimes known as Virtual Organizations). Grid technologies promise to change the way organizations tackle complex problems by offering unprecedented opportunities for resource sharing and collaboration. Grid technology can either significantly reduce the cost or time to produce results, or provide resources that are able to deliver services that cannot be economically delivered using conventional networked information systems. The implementation of a system on the computational grid platform for epidemiologic studies opens new perspectives for gathering data on large populations, and – as a consequence – would allow stratification of large scale metropolitan epidemiology studies.

B.1.2.3 ICT monitoring and reporting system.

Data represents an obstacle to progress not only because it is scattered across different repositories in different formats, standard and classification, but also because its rate of acquisition and experimental design is limited. Real time surveillance data are crucial to rapidly identify public health emergencies, understand

global trends and driving factors, feed realistic data-driven models to assess the impact on the population, optimize the allocation of resources to fight against them, and devise mitigation and containment measures to reduce economic, communication, transportation, and – more in general – social disruption (WHO-EPR; EISS; Jones et al., 2008). At the moment, however, acquisition of large scale data is not timely and, more importantly, not thought to inform models in real time. In general existing disease surveillance systems (GP sentinel) have several important limitations, in particular in their inability to provide information in real time, and on patterns of household transmission; in their lack of uniform standards for clinical definitions, that vary considerably between countries and even between reporters (EISS). Moreover, age-stratified rates of physician consultation may vary widely with different health care and health insurance systems. Especially for diseases as influenza-like-illness, only a minor (and unknown) fraction of all infected individuals sees a doctor, and frequently after a considerable delay, when a complication has occurred or in case a doctor's certificate is required (e.g. in Sweden such a certificate is not required until after 1 week). This is for instance the problem with the healthmap project put forward at MIT that considers data from heterogeneous sources but mainly due to report from health centers, thus neglecting most cases that do not seek medical help. Reporting rate may change unpredictably during an epidemic, making extrapolations of those statistics to the general population uncertain. Moreover, in many European countries the recruitment of sentinel GPs does not ensure proper sampling so that the geographic distribution of reporters does not faithfully represent the distribution of inhabitants, further complicating the attribution of observed cases to the population at risk. Existing surveillance systems also lack the flexibility to cope with new variants of existing pathogens that may result in atypical symptoms. These systems are also very vulnerable in the case of high prevalence and socially disruptive epidemics due to the limited capacity of hospitals and health care centres which induce biases in the number of visits per sentinel physician. In all cases, these limitations are crucially undermining the development of real-time data-driven modelling and forecast capabilities.

The project intends to overcome the limitation of the state of the art surveillance systems by proposing an innovative ICT approach based on Web2.0 tools. Starting from the successful experiences of internet-based monitoring systems (IMS) in the Netherlands and in Portugal (Influenzanet) which displayed high values in surveillance, epidemiological analysis and participant recruitment (Marquet et al., 2006; van Noort et al. 2007), the project plans to deploy an innovative real-time surveillance system across European countries. The IMS works with the Internet participation of the population to collect real-time information on the distribution of diseases through web-services. The collaborative participation of users is achieved through targeted communication and recruitment (Coutinho et al., 2004; Bettencourt-Dias et al., 2004). Graphic representation, processing and analysis of data on the progression of the disease, is provided in real time. In addition the project considers mobile telephone as enabling access technology so that larger fractions of the population can be involved in the real time data acquisition. The proposed IMS foresees for the first time the collaboration of epidemiologist and public health practitioners with modellers. The epidemiology teams will take care of defining "golden standard" for different diseases in order to have unified data across European countries. While influenza-like illnesses (ILI) are used in the early deployment of the system, the final IMS will consider other diseases and infections. Population-based real-time monitoring, under development in Sweden, promises further refinement of patient-initiated disease reporting using state-of-the-art telecommunication and Internet techniques, guaranteeing the link to the underlying population that generates the cases. The project will provide also the first comparative assessment of various surveillance methods and will test and calibrate the IMS by the epidemiology teams. By performing truly population-based disease surveillance (in a controlled sample of the population) in parallel with the IMS surveillance program, we will be able to shed better light on the issue of systematic errors in the rates. Sweden, with its efficient population administration, unique national registration numbers assigned to all residents immediately after birth or immigration, and a long-since established complete and rapidly/continuously updated computerized population register, offers exceptional opportunities to obtain random and thus

representative samples of the population. Ideally, the validation effort will result in correction factors that will allow us to re-calibrate the IMS data.

References

- Águas R, Gonçalves G, Gomes MGM (2006) *Lancet Infectious Diseases* 6, 112.
- Águas R, White LJ, Snow RW, Gomes MGM (2008) *Plos ONE* 3(3): e176 .
- Ajelli M, Merler S (2008) *PLoS ONE* 3(1): e1519.
- Ajelli M, Iannelli M, Manfredi P, Ciofi degli Atti ML (2008) *Vaccine* 26(13): 1697-1707.
- Albert R, Barabasi A-L (2000) *Rev. Mod. Phys.* 74, 47.
- Anderson RM, May RM (1991) *Infectious diseases of humans: Dynamics and control* (New York: Oxford University Press).
- Badii R, Politi A (1999) *Complexity, Hierarchical structures and scaling in physics.* (Cambridge University Press).
- Barrat A, Barthelemy M, Pastor-Satorras R, Vespignani A (2004) *Proc. Natl. Acad. Sci.* (USA) 101, 3747.
- Barrett CL et al. (2000) *Technical Report LA-UR-00-1725*, Los Alamos National Laboratory.
- Barthélemy M, Barrat A, Pastor-Satorras R, Vespignani A (2005) *J. Theor. Bio.* 235, 275.
- Bettencourt-Dias M, Coutinho AG and Araújo SJ (2004) *Comunicação e Sociedade* 6:89-112
- Binder S, Levitt AM, Sacks JJ, Hughes JM (1999) *Science* 284, 1311.
- Brockmann D, Hufnagel L, Geisel T (2006) *Nature* 439, 462.
- BTS, Bureau of Transportation Statistics, http://www.bts.gov/
- Camitz M, Liljeros F (2006) *BMC Med* 4, 32.
- Chowell G, Hyman JM, Eubank S, Castillo-Chavez C (2003) *Phys. Rev. E* 68, 066102.
- Cohen R, Havlin S, and ben-Avraham D (2003) *Phys. Rev. Lett.* 91, 247901.
- Ciofi degli Atti ML, Merler S, Rizzo C, Ajelli M, Massari M, Manfredi P, Furlanello C, Scalia Tomba G, Iannelli M (2008) *PLoS ONE* 3(3): e1790.
- Colizza V, Barrat A, Barthelemy M, Vespignani A (2006) *Proc. Natl. Acad. Sci.* (USA) 103, 2015.
- Colizza V, Barrat A, Barthelemy M, Valleron A-J, Vespignani A (2007a) *PLoS Med.* 4: e13.
- Colizza V, Barrat A, Barthelemy M, Vespignani A (2007b) *BMC Med.* 5, 34.
- Cooper BS, Pitman RJ, Edmunds WJ, Gay NJ. (2006) *PLoS Med.* 3: e12.
- Coutinho AG, Araújo SJ and Bettencourt-Dias M, (2004) *Comunicação e Sociedade* 6:113-134
- Couto F, Silva M, Lee V, Dimmer E, Camon E, Apweiler R, Kirsch H, and Rebholz- Schuhmann D (2006) *Journal of Biomedical Discovery and Collaboration*.
- Daley DJ, Gani J (1999) *Epidemic Modelling* (Cambridge University Press, Cambridge).
- da Silva FAB, Gagliardi HF, Gallo E, Madope MA, Cavicchiolli Neto V , Torres Pisa I and Alves D (2007) *Studies in Health Technology and Informatics* v. 126, p. 197-206.
- Daszak P, Cunningham AA & Hyatt AD (2000) *Science* 287, 443–449.
- de Blasio BF, Svensson A, Liljeros F (2-007) *Proc. Natl. Acad. Sci.* (USA) 104, 10762-7.
- Diekmann O, Heesterbeek JAP (2000) *Mathematical epidemiology of infectious diseases: Model building, analysis and interpretation* (New York: John Wiley and Sons).
- Dobson (2008) in (Keeling and Rohani).
- Dorogovtsev SN, Mendes JFF (2003) *Evolution of Networks: From Biological Nets to the Internet and WWW* (Oxford Univ. Press, Oxford).
- Dye C (2008) *Science* 319, 766.
- Eames, KTD & Keeling MJ (2002) *Proc. Natl Acad. Sci. USA* 99, 13330-13335.
- Eames KTD (2008) *Theor. Popul. Biol.* 73, 104–111.
- EGEE Project (2008) http://www.eu-egee.org/. Accessed April 1, 2008.
- EISS. European Influenza Surveillance Scheme, http://www.eiss.org/index.cgi
- Eubank S, Guclu H, Kumar VSA, Marathe MV, Srinivasan A, Toroczkai Z, Wang N (2004) *Nature* 429, 180.
- EUPHIN, http://ec.europa.eu/idabc/en/document/2259/5926
- Ferguson et al. (2003) *Nature* 425, 681.
- Ferguson NM, Cummings DAT, Cauchemez S, Fraser C, Riley S et al. (2005) *Nature* 437, 209.
- Ferguson NM, Cummings DAT, Fraser C, Cajka JC, Cooley PC, et al. (2006) *Nature* 442, 448.
- Foster I (2002) *GRID today* vol. 1, no. 6, 2002. Retrieved April 1, 2008 from http://www.gridtoday.com/02/0722/100136.html.

- Foster I (2005) *Globus Toolkit Version 4: Software for Service-Oriented Systems. IFIP International Conference on Network and Parallel Computing*, Springer-Verlag LNCS 3779, pp. 2-13.
- Gagliardi HF, da Silva FAB, and Alves D. *Automata Network Simulator Applied to the Epidemiology of Urban Dengue Fever.* Alexandrov et al. (Eds.): ICCS 2006, LNCS 3993, pp. 297 – 304, 2006.
- Gallos L, Liljeros F, Argyrakis P, Bunde A, Havlin S (2007) *Phys. Rev. E* 75, 045104.
- Germann TC, Kadau K, Longini IM, Macken CA (2006) *Proc. Natl. Acad. Sci.* (USA) 103, 5935.
- GIS. Geographic Information Systems, http://www.gis.com
- Globus Alliance (2008) http://www.globus.org Accessed April 1, 2008.
- Gomes MGM, Medley GF, Nokes DJ (2002) *Proc. R. Soc. Lond.* B 269, 227.
- Gomes MGM, White LJ, Medley GF (2004a) *J. Theor. Biol.* 228, 539.
- Gomes MGM, Franco AO, Gomes MC, Medley GF (2004a) *Proc. R. Soc. Lond.* B 271, 617.
- Gomes MGM, Margheri A, Medley GF, Rebelo C (2005) *J. Math. Biol.* 51, 414.
- Guimera R, Mossa S, Turtschi A, Amaral LAN (2005) *Proc. Natl. Acad. Sci.* (USA) 102, 7794.
- Halloran ME, Longini IM, Nizam A, Yang Y (2002) *Science* 298, 1428.
- Hufnagel L, Brockmann D, Geisel T (2004) *Proc. Natl. Acad. Sci.* (USA) 101: 15124.
- Influenzanet: De Grote Griep Meting (Netherlands/Belgium), http://www.degrotegriepmeting.nl/; Gripenet (Portugal), http://www.gripenet.pt; Influweb (Italy), http://www.influweb.it
- INFTRANS, http://www.inftrans.org/default.aspx
- IRIDE, http://iride.cineca.org
- Jones KE et al. (2008) *Nature* 451, 990.
- Keeling MJ, Rohani P (2008) *Modeling infectious diseases in humans and animals* (Princeton University Press).
- Kinchin AI (1957) *Mathematical foundation of Information Theory*. (Dover NY).
- King DA, Peckham C, Waage JK, Brownlie J&Woolhouse MEJ (2006) *Science* 313, 1392–1393 .
- Liljeros F, Edling CR, Amaral LAN, Stanley HE, Aberg Y (2001) *Nature* 411, 907.
- Lloyd SL, May RM (2001) *Science* 292, 1316.
- Longini IM, Nizam A, Xu S, Ungchusak K, Hanshaoworakul W, et al. (2005) *Science* 309, 1083.
- Lopez E, Parshani R, Cohen R, Carmi S, Havlin S (2007) *Phys. Rev. Lett.* 99, 188701.
- Madar N, Kalisky T, Cohen R, ben-Avraham D, Havlin S (2004) *Eur. Phys. J. B* 38, 269.
- Marquet RL, Bartelds AIM, van Noort SP, Koppeschaar CE, Paget J, Schellevis FG, van der Zee J (2006) *BMC Public Health* 6, 242.
- Massad E, Chen M, Ma S, Struchiner CJ, Stollenwerk N, Aguiar M (2008) *Applied Mathematics and Computation* 159,376-381.
- MODELREL, http://ec.europa.eu/health/ph_projects/2003/action2/action2_2003_03_en.htm
- Morens DM (1998) *Pacific Health Dialog* 5, 147.
- Morens DM, Folkers GK, Fauci AS (2004) *Nature* 430, 242.
- Morse, *S. S. in Emerging Viruses* (ed. Morse, S. S.) 10–28 (Oxford Univ. Press, New York, 1993).
- Mossong J et al. (2008) *PLoS Med* 5(3): e74
- OASIS Consortium (2008). http://www.oasis-open.org. Accessed April 1, 2008.
- OGF - Open Grid Forum (2008). http://www.ogf.org. Accessed April 1, 2008.
- Onnela J-P, Saramäki J, Hyvönen J, Szabó G, Lazer D, Kaski K, Kertész J, Barabási A-L (2007) *Proc. Natl. Acad. Sci.* (USA) 104, 7332.
- Pastor-Satorras R, Vespignani A (2003) *Evolution and Structure of the Internet: A Statistical Physics Approach* (Cambridge Univ. Press, Cambridge, UK).
- Pastor-Satorras R, Vespignani A (2001) *Phys. Rev. Lett.* 86, 3200.
- Patz JA et al. (2004) *Environ. Health Perspect.* 112, 1092–1098.
- Peiris JSM et al. (2003) *New England Journal of Medicine* 349, 2431.
- Pitman RJ, Cooper BS, Trotter CL, Gay NJ, Edmunds WJ (2005) *BMJ* 331(7527):1242-3.
- POLYMOD, http://ec.europa.eu/research/fp6/ssp/polymod_en.htm
- Riley S (2007) *Science* 316, 1298.
- Schneeberger A, Mercer CH, Gregson SA, Ferguson NM, Nyamukapa CA, Anderson RM, Johnson AM, Garnett GP (2004) *Sex. Trans. Dis.* 31, 380.
- Smolinski MS, Hamburg MA, Lederberg J (2003) *Microbial Threats to Health: Emergence, Detection, and Response* (National Academy Press, Washington DC).
- Stollenwerk N, Martins J, Pinto A (2007) *Phys. Lett.* A 371, 379-388.

- Stone L, Shulgin B and Agur Z (2000) *Mathematical and Computer Modelling* 31:207-215.
- Stone L, Olinky R and Huppert A (2007) *Nature* 446: 533-536.
- Taylor LH, Latham SM & Woolhouse MEJ (2001) *Phil. Trans. R. Soc. Lond.* B 356, 983–989.
- van Noort SP, Lourenço J, Rebelo de Andrade H, Muehlen M, Gomes MGM (2007) *Eurosurveillance Monthly* Volume 12, Issue 7-8.
- Weiss RA & McMichael AJ (2004) *Nature Med.* 10, S70–S76.
- WHO-EPR. World Health Organization – Epidemic and Pandemic Alert and Response. http://www.who.int/csr/en/
- WHO-SARS. World Health Organization – Severe Acute Respiratory Syndrome. http://www.who.int/topics/sars/en/
- Woolhouse MEJ & Gowtage-Sequeria S (2005) *Emerging Infect. Dis.* 11, 1842–1847.
- Zurek WH (1990). *Complexity, Entropy and the Physics of Information.* (Addison Wesley Publishing Company).

B.1.3 S/T methodology and associated work plan

B.1.3.1 Overall Strategy and general description

The project revolves around six distinct scientific work packages (WP1-WP6) aimed at providing a virtuous feedback cycle between tool development, data collection, analysis and modelling. Parallel scheduling of the work-packages is necessary to jump start the cycle and the Inter-WP validation. The research plan is structured so as to foster a fruitful interplay between the various components of the project. WP1 and WP2 are aimed at exploring theoretical issues in the area of epidemic modelling in complex, multiscale systems, structured populations and in the presence of the dynamical interplay between social and technological factors, seasonality and climate, health policies implementations. WP3 and WP4 are devoted to the collection and sharing of data on a computational platform and have a two way continuous exchange with WP1 and WP2 of data and algorithms. WP5 and WP6 is aimed at the developing, set-up and deployment of innovative web monitoring and data gathering tools that provide a continuous stream of data to WP3-WP4 and is informed by a constant feedback on the modelling needs in terms of data gathering by WP1 and WP2. The project revolves around a relatively small number of WPs sign of the common research agenda of the consortium teams that work in a coordinated way on the various tasks. This favours a closer interchange of ideas and knowledge among the groups and the various components of the project. The methodology is clearly truly interdisciplinary.

Risk description	Evaluation	Resolution
Consortium has no harmony/ too large	*Impact High, Prob. Low* Should this problem occur its impact on the project would be significant. However the probability of occurrence is low due to previous collaborations, background, partners experience.	In case of need, the chairs will work closely with specific partners in order to ensure their working in harmonisation. In rare cases, if it will not solve the problem, and partner is seriously defaulting, they will be excluded from the consortium and replaced.
Poor quality of deliverables and delay in meeting the deadlines.	*Impact High. Prob. Low* *Partners have extensive experience in the field and are recognized top rate researchers with a strong record of achievements.*	The progress of the project will be assessed at frequent intervals as detailed in the project management.
Failure to get relevant real world data sets	*Impact High, Prob. Infinitesimal* Partners have access to a wide array of sources of data. We integrate data from the IMS.	Monitoring data collection progress to be able to develop new sources in time.
Failure to develop adequate models and tools	*Impact Very High, Prob. Very Low.* While some of the proposed tasks may fail, the variety of issues and facets considered will lead to overall good results.	Continuous monitoring by project coordinator to ensure that failed approaches are abandoned in time to try new ideas.
Amount of data too large to be handled conveniently by the computational and data sharing platform.	*Impact High , Prob. Low* During the project the use of Grid technology will enable large-scale data-intensive computing, management and storage.	Data sharing, management, and integration will be given high priority and be continuously monitored. Building on consortiums experience and access to various possible technologies.
Failure to integrate data and models in a large scale computational framework	*Impact high. , Prob Low* The consortium partners have extensive experience in data models integration.	The validation and feedback cycle will allow us to learn starting with simpler integration. Stepwise integration will mean that even if we fail to integrate all approaches some integration will be achieved.
Failure to involve enough participants in the IMS	*Impact high, Prob Low* We have over five years of experience in NL, B and PT and more than 60.000 accounts. There is no reason to expect that in 'new' IMS countries this will be different even though internet penetration rates may differ from country to country	Proven recruitment strategies (media exposure) are to be pursued. New strategies as well provided they work: consortium partners will exchange their 'best practice' experiences in these.

Panel 1: List of identifiable risks, their impact and contingency plan. In yellow is highlighted the key risk of the project.

Each WP includes several core disciplines expertise and it is anchored to the epidemiology area by the presence of mathematical biologists, epidemiologist and public health experts. These groups will provide the main research questions, the basic disease and parameters choices and the relevant complex features of epidemiological systems as well as their contribution in the development of cross-fertilized and novel approaches targeted in the WPs.

A project of such an extent requires a constant monitoring of the possible problems arising during the course of the research activities. While monitoring will be ensured by the project leadership, the annual reviews and the external advisory board, a list of significant risks can be already identified in the project. In the panel 1 we provide a list of identifiable risks, their likely impact and the resolution plan that is possible to envisage a at this stage.

WP 7 is management. This project is initiated by a group of senior scientists, working at the best research institutions in Europe. The Institute of Scientific Interchange provides the management of the project and the coordination of the consortium. Finally WP8 is devoted to outreach and dissemination activities.

In summary, the project is structured in the following work packages:

1. Work package 1 – **Populations models and contact networks (WP leader: L. Stone)**
2. Work package 2 – **Spatially structured models and human mobility (WP leader: D.Brockmann)**
3. Work package 3 – **Information platform (WP leader: M.J.Silva)**
4. Work package 4 – **Epidemic Modelling Platform (WP leader: A. Vespignani)**
5. Work package 5 - **ICT monitoring and reporting system (WP leader: R. Smallenburg)**

6. Work package 6 – **Reporting systems comparative analysis and validation (WP leader: O.Nyren)**
7. Work package 7 – **Management (WP leader: A.Vespignani)**
8. Work package 8 – **Dissemination, collaboration and exploitation (WP leader: A.Vespignani)**

Each WP has a WP-leader that supervises the work progress and assesses and corrects deviations from project goals. The WP-leader is also responsible for the coordination with the activities of other WPs.

B 1.3.2 Timing of work packages and their components

The WP-leaders will make sure that the different WPs and their principal components are timed according to the Gantt chart below:

		Year 1			**Year 2**			**Year 3**			**Year 4**		
		M4	M8	M12	M16	M20	M24	M28	M32	M36	M40	M44	M48
WP1	**Population models and contact networks**												
Task 1				**D1.1**									
Task 2				**D1.1**									
Task 3				**D1.1**									
Task 4				**D1.1**									
Task 5				**D1.1**									
Task 6										**D1.3**			
Task 7										**D1.4**			
Task 8													**D1.5**
Task 9				**D1.1**									**D1.5**
Task 10										**D1.4**			
Task 11							**D1.2**						
Task 12													**D1.5**
WP2	**Spatially structured models and human mobility**												
Task 1				**D2.1**									
Task 2				**D2.1**									
Task 3							**D2.2**			**D2.4**			
Task 4							**D2.2**			**D2.4**			
Task 5							**D2.2**			**D2.4**			
Task							**D2.2**			**D2.4**			

6													
Task 7										D2.3			D2.5
Task 8										D2.3			D2.5
Task 9										D2.3			D2.5
WP3	**Information platform**												
Task 1			D3.1										
Task 2			D3.1										
Task 3				D3.2		D3.3				D3.4			D3.6
Task 4										D3.4 D3.5			D3.6
WP4	**Epidemic Modelling Platform**												
Task 1						D4.2							
Task 2				D4.1									
Task 3						D4.2			D4.3		D4.4		D4.5 D4.6
Task 4											D4.4		D4.5 D4.6
Task 5											D4.4		D4.5 D4.6
WP5	**ICT monitoring and reporting system**												
Task 1				D5.1									
Task 2						D5.3							D5.7
Task 3						D5.3							D5.7
Task 4						D5.3							D5.7
Task 5									D5.5				D5.7
Task 6									D5.5				D5.7
Task 7						D5.4							
Task 8									D5.6				
Task 9													D5.7
Task 10				D5.2									
WP6	**Reporting systems comparative analysis and validation**												
Task 1							D6.2						
Task 2				D6.1									
Task 3							D6.3						

Task 4										D6.4			
Task 5										D6.4			
Task 6													D6.5
WP7	**Management**												
7.1				D7.1			D7.2			D7.3			D7.4
7.2				D7.5			D7.6			D7.7			D7.8
WP8	**Dissemination, collaboration and exploitation**												
Task 1		D8.1											
Task 2			D8.2				D8.3					D8.4	
Task 3							D8.3					D8.4	D8.5 D8.6
Task 4												D8.4	D8.5 D8.6

B.1.3.3 Work package list Overview

Work package list

Work package No[1]	Work package title	Type of activity[2]	Lead partic no.[3]	Lead partic. short name	Person-months[4]	Start month[5]	End month[5]
1	*Population models and contact networks*	RTD	3	TAU	184.5 (61)	1	48
2	*Spatially structured models and human mobility*	RTD	4	MPG	171.5 (95)	1	48
3	*Information platform*	RTD	12	FFCUL	128 (89)	1	48
4	*Epidemic Modelling Platform*	RTD	1	ISI	160 (92)	1	48

1 Workpackage number: WP 1 – WP n.

2 Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results and coordination activities.

3 Number of the participant leading the work in this work package.

4 The total number of person-months allocated to each work package.

5 Measured in months from the project start date (month 1).

5	*ICT monitoring and reporting system*	RTD	5	AIBV	239.5 (30)	1	48
6	*Reporting systems comparative analysis and validation*	RTD	7	SMI	66 (82)	1	48
7	*Management*	MGT	1	ISI	40 (28)	1	48
8	*Dissemination, collaboration and exploitation*	OTHER	1	ISI	50 (47)	1	48
	TOTAL				1039.5 (524)		

Person-months in the table contain 2 numbers: the first number corresponds to the number of person months (PMs) derived from the EC requested contribution, whereas the second – in brackets – corresponds to the number of PMs not from EC contribution.

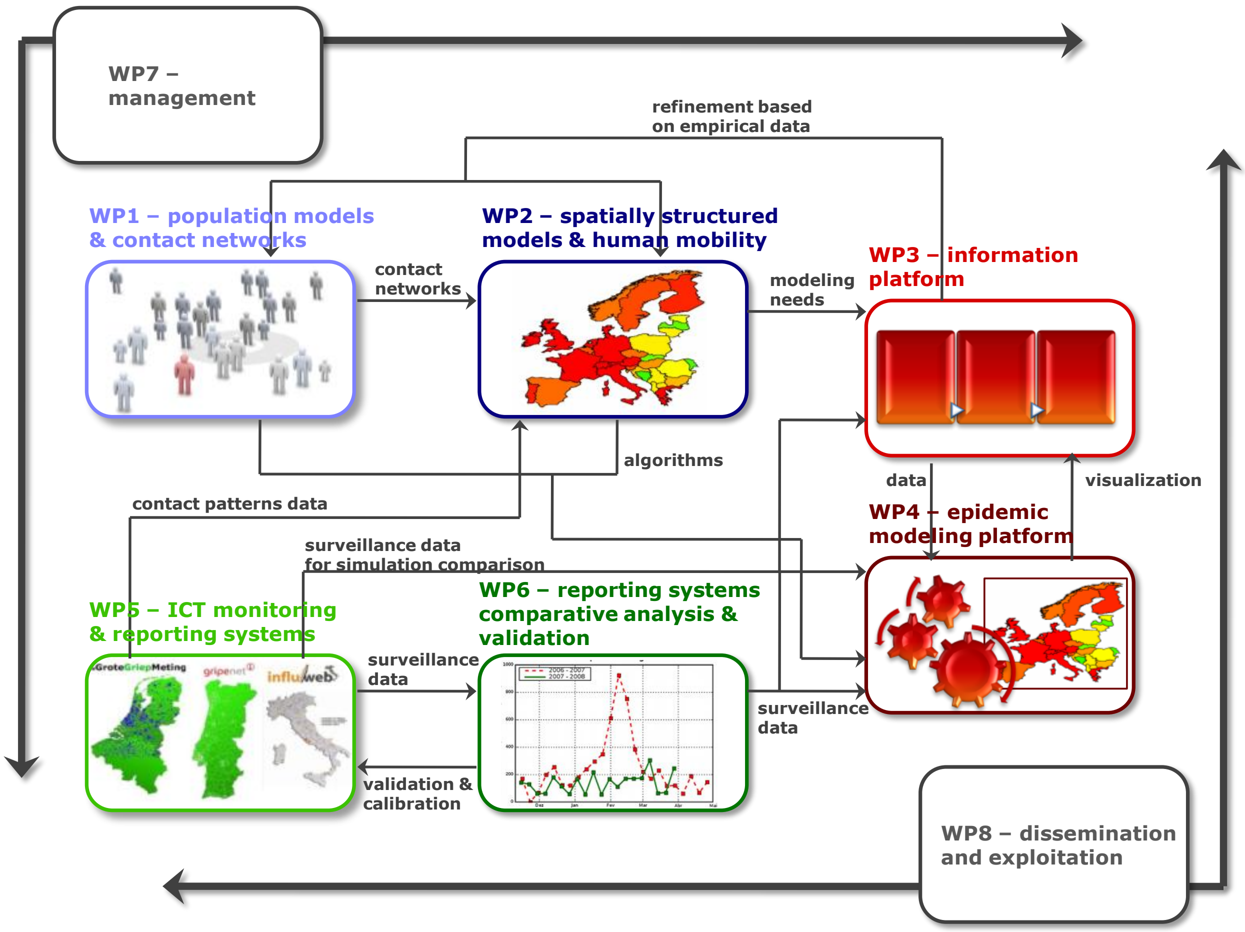

Diagram 2: Graphical presentation of the project components

The diagram above sketches the information flow and functional dependences among the different work packages composing the project. The diagram also that all WPs units bear to the Management (WP7) and Dissemination and exploitation (WP8) WPs.

B1.3.4 Deliverables List

List of Deliverables – to be submitted for review to EC[6]

Del. no.[7]	**Deliverable name**	**WP no.**	**Lead bene-ficiary**	***Estimated indicative person-months***	**Nature[8]**	**Dissemination level[9]**	**Delivery date[10] (proj. month)**
1.1	Analysis of dynamics on clustered contact networks.	1	TAU	36 (12)	O	PU	Month 12
1.2	Practical transmission measures in the presence of reinfection.	1	TAU	18 (6)	O	PU	Month 24
1.3	Models of disease transmission under seasonality and other external drivers.	1	TAU	36 (12)	O	PU	Month 36
1.4	Models of spread, impact and evolution of vector-borne pathogens, including the demography and ecology of host species.	1	TAU	36 (12)	O	PU	Month 36
1.5	Model parameterization, simulation, prediction and quantification of uncertainly.	1	TAU	58.5 (19)	R	PU	Month 48
2.1	Implementation of multi-scale proxies networks for human mobility networks from online data-sources: www.geocaching.com, www.bookcrossing.com, www.wheresgeorge.com, www.eurobilltracker.com.	2	MPG	31 (17)	O	PU	Month 12
2.2	Theoretical foundation and mathematical description of network-network systems, i.e. spatially embedded contact networks	2	MPG	47 (26)	R	PU	Month 24

6 In a project which uses 'Classified information[6]' as background or which produces this as foreground the template for the deliverables list in Annex 7 has to be used

7 Deliverable numbers in order of delivery dates. Please use the numbering convention <WP number>.<number of deliverable within that WP>. For example, deliverable 4.2 would be the second deliverable from work package 4.

8 Please indicate the nature of the deliverable using one of the following codes:
R = Report, **P** = Prototype, **D** = Demonstrator, **O** = Other

9 Please indicate the dissemination level using one of the following codes:
PU = Public
PP = Restricted to other programme participants (including the Commission Services).
RE = Restricted to a group specified by the consortium (including the Commission Services).
CO = Confidential, only for members of the consortium (including the Commission Services).

10 Measured in months from the project start date (month 1).

	and empirical validation by case study of respiratory diseases in the UK.						
2.3	Development of theory and stability analysis for limited path multiscale transportation networks: Networks that take into account effective multiple length scales of transportation, and their couplings. Rules for the link strengths between contacts that take into account the multiscale problem.	2	MPG	31 (17)	R	PU	Month 36
2.4	Spatially embedded networks: Specific rules for contact in the context of spatial embedding. Properties of the networks subjected to such spatial embedding constraints.	2	MPG	15 (8.5)	R	PU	Month 36
2.5	The development of order parameters and quantitative indicators for predictability in complex multi-scale epidemiological dynamical systems.	2	MPG	47.5 (26.5)	R	PU	Month 48
3.1	Report - Meta-model initial specification , catalogue of relevant data, platform requirements.	3	FFCUL	13 (9)	O+ R	CO	Month 8
3.2	Prototype of the Epidemic Marketplace Platform with an initial set of epidemiological databases integrated available to project participants.	3	FFCUL	39 (25)	P	CO	Month 12
3.3	Public release of the Epidemic Marketplace Platform.	3	FFCUL	26 (17)	D	PU	Month 20
3.4	Report for the Epidemic Marketplace Platform after release, describing changes and new implemented features, new data sources integrated with the platform, results of user surveys and usage statistics.	3	FFCUL	13 (10)	R	CO	Month 36
3.5	Report – Epidemic data ontology.	3	FFCUL	13 (10)	R	PU	Month 36
3.6	Report – Final specification of the Epidemic Marketplace Platform and evaluation results.	3	FFCUL	24 (18)	R	PU	Month 48
4.1	Static single layer visualization techniques (choropleth maps, distortions, dasymetric maps) and simple mashups.	4	ISI	14 (8)	P	PU	Month 12
4.2	Prototype modelling suite of the Epidemic Modelling Platform programmed including contact patterns and population mobility as emerging from WP1 and WP2, with documentation.	4	ISI	39 (21)	P	CO	Month 20
4.3	Public release of the Epidemic Modelling Platform.	4	ISI	26 (14)	D	PU	Month 32

4.4	Report for the Epidemic Modelling Platform after release, describing changes and new implemented features, new visualizations and modelling algorithms integrated with the platform, results of user surveys and usage statistics.	4	ISI	13 (8)	R	PU	Month 40
4.5	Application of Epidemic Modelling Platform to seasonal influenza modelling in (i) participating countries; (ii) Europe; (iii) worldwide. Comparison with influenza surveillance data and harmonization of European countries preparedness plans on early and efficient responses to health emergencies.	4	ISI	39 (21)	O	PU	Month 48
4.6	Report – Final specification of the Epidemic Modelling Platform, evaluation results, academic papers.	4	ISI	29 (20)	R+ O	PU	Month 48
5.1	Design of the ‘golden standard’, design and implementation of an internet database with English language documents.	5	AIBV	34 (4)	O+ D	PU	Month 12
5.2	Extension of IMS for collating contact pattern information and household influenza transmission data.	5	AIBV	17 (3)	P	PU	Month 12
5.3	Tests run in 2009.	5	AIBV	34 (4)	O+ R	PU	Month 20
5.4	Extension of IMS by mobile phones’ data gathering.	5	CREAT E-NET	30 (4)	P	PU	Month 20
5.5	Tests run in 2010.	5	AIBV	34 (4)	O+ R	PU	Month 32
5.6	Design and implementation of software for contacts patterns detections.	5	CREAT E-NET	32 (4)	P	PU	Month 32
5.7	Gradual implementation of IMS and its internet database from 2010 onwards: well operating systems in five ‘new’ countries and in the four ‘old’ countries in 2013.	5	AIBV	58.5 (7)	P	PU	Month 48
6.1	A fully functioning technical infrastructure for the PBA surveillance.	6	SMI	16 (20)	D	PU	Month 12
6.2	A fully functioning and tested IMS in operation in Sweden.	6	SMI	14 (14)	P	PU	Month 24
6.3	The PBA cohort established.	6	SMI	8 (9)	O	PU	Month 24
6.4	The validation study of the PBA surveillance concluded, and the digitalized dataset delivered.	6	SMI	14 (19)	O	PU	Month 36
6.5	Academic papers on the validity of the PBS and on the concordance between results from IMS, PBA,	6	SMI	14 (20)	R	PU	Month 48

	sentinel system and laboratories.						
7.1	Yearly management report.	7	ISI	6 (3)	R	PU	Month 12
7.2	Yearly management report.	7	ISI	6 (3)	R	PU	Month 24
7.3	Yearly management report.	7	ISI	6 (3)	R	PU	Month 36
7.4	Yearly management report.	7	ISI	6 (3)	R	PU	Month 48
7.5	Yearly activity/assessment report	7	ISI	4 (4)	R	PU	Month 12
7.6	Yearly activity/assessment report	7	ISI	4 (4)	R	PU	Month 24
7.7	Yearly activity/assessment report	7	ISI	4 (4)	R	PU	Month 36
7.8	Yearly activity/assessment report	7	ISI	4 (4)	R	PU	Month 48
8.1	Project presentation report.	8	ISI	1 (2)	R	PU	Month 4
8.2	Project web site.	8	ISI	3 (4)	D	PU	Month 8
8.3	Mid-term workshop.	8	ISI	3 (4)	O	PU	Month 24
8.4	Final year workshop.	8	ISI	3 (4)	O	PU	Month 44
8.5	Final non-technical report on the project.	8	ISI	4 (4)	R	PU	Month 48
8.6	Yearly dissemination, collaboration and exploitation report		ISI	8 (6)	R	PU	Month 12
8.7	Yearly dissemination, collaboration and exploitation report		ISI	8 (6)	R	PU	Month 24
8.8	Yearly dissemination, collaboration and exploitation report		ISI	8 (6)	R	PU	Month 36
8.9	Yearly dissemination, collaboration and exploitation report		ISI	8 (6)	R	PU	Month 48
8.10	Preparation of collected papers book (edited by the project Chairs) highlighting the major advances and specific contributions of the project to the field	8	ISI	4 (5)	R	PU	Month 48
			TOTAL	1039.5 (524)			

B.1.3.5 Work package description

WP 1 – Population models and contact networks

Work package number	1	**Start date or starting event:**		Month 1			
Work package title	**Population models and contact networks**						
Activity type[11]	RTD						
Participant number	**3**	2	6	9	12		
Participant short name	**TAU**	FGC-IGC	LSHTM	BIU	FFCUL		
Person-months per beneficiary	96	52	25.5	30	42		

Objectives

As there is a large gap between the classical epidemiological theory with its stylized models, and complex real world disease dynamics, this work package intends to create new Theoretical Foundations that are intended to help significantly fill the gap. Four central themes will be addressed in WP1.

The first theme of this WP concerns population contact networks which characterize the non-random manner in which individuals in a large population come into contact in the form of a connectivity matrix or graph. This work will determine how heterogeneities due to population aggregations and spatial structuring control both epidemic size, extinction thresholds as well as competition and evolution between disease strains. Classical theory has largely been concerned with random networks structure, while WP1 aims to push this to more realistic scenarios. The goal is the derivation of new mathematical models that on the one hand are not too large, so that they remain analytically tractable, yet nevertheless accurately characterize far better the complex dynamics of realistic large-scale heterogeneous systems.

The second theme is concerned more with dynamical temporal aspects of populations; in particular, the role of seasonality and other external environmental drivers. Seasonality is a driving force that has major impact on the spatio-temporal dynamics of natural systems and their populations. This is especially true for the transmission of common infectious diseases (eg., influenza, measles, chickenpox**,** pertussis), and of great relevance for host-parasite relationships in general. Theoretical studies have shown that seasonal forcing can be responsible for inducing complex population dynamics such as higher order cycles, resonances and deterministic chaos. These complex responses can easily mask any simple underlying mechanistic processes that might otherwise help in forecasting future epidemics. Based on recent work, we intend to develop a modelling framework that gives new insights into these processes, as well as leading to an epidemic

[11] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

prediction scheme.
The third theme deals with the prevention of disease spread through vaccination and containment strategies. Optimized immunization strategies need to be devised. Typically, only a fraction of the population can be subjected to intervention due to limited time and resources. We will consider a range of intervention strategies based on immunization or quarantine of individuals in two situations: when the contact network is known, and when it is not known or known only partially. The strategies studied are based on a set of new methods and ideas related to recent discoveries in complex networks research.
The fourth theme deals with models of reinfection. Vaccination against childhood infectious diseases has been a huge success. The unifying feature of this class of infections is that acquired immunity is highly protective and long lasting, so that recovered or vaccinated individuals are unlikely to be reinfected. However, many pathogens have evolved a variety of ways to circumvent immunity: persistence at reduced activity (*Mycobacterium tuberculosis*, *Plasmodium* spp), suppression of the immune system (HIV), or antigenic variation (influenza virus, respiratory syncytial virus, rotavirus, dengue, *Bordetella pertussis*, *Plasmodium falciparum*). These immune evasion mechanisms are common, and often work together to determine the effective protection against reinfection. A further complication is that, besides reducing reinfection rates, immunity often influences disease outcome without impeding pathogen replication and transmission. In influenza, pertussis and malaria, for example, symptoms range from very mild (or virtually absent) to very severe and life threatening, with reduced symptoms being attributed to immunity induced by previous exposures. In dengue, by contrast, heterologous immunity has been linked to more severe symptoms. As asymptomatic infectious are typically unreported, empirical relationships between such elaborate host-pathogen interactions and the associated epidemiological patterns are impossible to deduce. While relatively simple mathematical models remain first line tools, research benefits immensely by the availability of more flexible computer modelling approaches, combining the dynamics of infection, immunity, pathogen ecology, and confrontation with available data.

In addition, we will develop the necessary methodologies to parameterize the models developed in this work package from real data. This final task is transversal to all theme.

Description of work

Theme I: Contact Networks (LSHTM, TAU)

Task 1. Heterogeneous individuals and interactions: When using networks to visualise interactions within a population, it immediately becomes clear that not all individuals behave in the same way; for instance, there are marked heterogeneities in the number of contacts and many different *types* of interactions – such as those taking place at home or in the workplace, those that are strong and frequently repeated, as well as those that are short-lived or infrequent.. This variation within the population will be included in models and methods will be developed that identify high-risk individuals and potential superspreaders.

Task 2. Contact tracing: Contact tracing, whereby the contacts of infected individuals are sought for treatment or isolation, is a powerful intervention strategy, allowing effort to be focussed towards those areas of a contact network that are known to be at risk. There is different cost and different efficiencies in implementing contact tracing in different settings, and models will be useful to determine which links are most worthy of limited resources.

Task 3. Networks and public health: Not only infection but also public health messages can be passed through social networks. An understanding of the social environment of individuals is vital to understand their response to health campaigns and their likely behaviour in the case of an outbreak.

Task 4. Networks and evolution: The local nature of interactions within a human mixing network provides an environment for pathogens very different from a homogeneously mixed population. Models will be used to explore the possible impact of human social behaviour on the competition and evolution of emerging pathogens.

Task 5. Clustered networks: A key result addressing heterogeneity in transmission rates is the so-called CV^2 rule: an epidemic will occur only if $\boldsymbol{R_0 = \bar{R}(1 + CV^2) > 1}$, where CV is related to the coefficient of variation of individuals' contact rates and $\bar{R}$ is the reproductive number of the disease under homogeneous contact

structure. This previous work will be revisited by examining the effects of clustering on network dynamics, as related to the number of "triangles" in a network i.e., where "a friend of a friend is also your friend". As distinct from other attempts by pair-approximation approaches, generating function techniques from probability theory will be used to characterize the effects of clustering on epidemic dynamics.

Theme II: Seasonality and other external environmental drivers(FGC-IGC, FFCUL, TAU)

Task 6 Epidemic predictions in seasonally forced systems: To gain insight into the nonlinear dynamics of recurrent flu epidemics, we analyze the seasonally forced SIRC influenza model with temporary immunity. As opposed to susceptible, cross-immune individuals may recover after encountering the flu virus without passing through the Infectious stage. Based on previous work, we intend to determine clear analytical conditions for predicting the occurrence of either an epidemic outbreak next year, or a ‘skip’—a year in which an epidemic fails to initiate. The threshold depends on the population’s susceptibility and cross-immunity measured after the last outbreak and the rate at which new susceptible individuals are recruited into the population. The goal is to clarify the relationship through mathematical analysis.

Task7 Demographic and ecological interactions of host populations: Demographics are important when the duration of disease cannot be separated from the host's life expectancy. The inflow of new susceptibles provides the fuel for ongoing disease transmission. We will identify and review basic mechanisms that induce (i) multistability of different endemic prevalence levels and (ii) oscillatory disease dynamics. Aspects that will be considered include nonlinear transmission processes, different pathogen strains, host demographics and depensations, seasonality, lethality, immunity and latency etc.Many diseases are transmitted by animal vectors and involve (multiple) reservoirs in their life cycle. Modelling therefore requires us to address the demography of the vector population as well as its ecology. We propose to begin a systematic classification of these predator-prey models including various pathways of disease transmission.

Theme III: Development of effective intervention strategies with or without the knowledge of the contact network (BIU, TAU).

Task 8. Interventions without contact network knowledge: Intervention strategies that are effective when contact information is lacking are tremendously useful. Such strategies invariably require some contact information to become available easily in order to correctly identify the best targets for intervention. We will develop strategies based on novel mechanisms exploiting the contact pattern heterogeneity (Acquaintance Immunization method in Cohen et al. Phys Rev. Lett. 2003).

Task 9. Interventions when the contact network is known. In this case, it is possible to globally optimize the strategy to attack the most important nodes in order to stop the spread of the disease. For this, we will apply methods based on direct network knowledge, which are the most powerful. One such method is based on the problem of efficient graph partitioning This strategy can be adapted from work in computer science. Although the formal problem is NP-complete, preliminary work shows that this separation can be done in a pseudo-optimal way through, and the method performs better in model networks than any available immunization strategy currently known. A second method we intend to use is based on the k-core decomposition of a network, which identifies the level of peripheral vs. central role of a node. By eliminating the most central nodes of the network (deepest k-core), model systems have been shown to collapse extremely rapidly, providing good justification to try this method as a possibly efficient immunization strategy.

Task 10. Limiting effective path length: The ability of a pathogen to infect is related to factors specific of the host (e.g., susceptibility, immune response), factors of the pathogen (e.g., infectivity, evolution) and the transmission environment (e.g., season of the year). Time variations of some of these factors such as evolution of the pathogen, or a change in season, represent constraints of the problem and influence the evolution of an epidemic (see WP2). Based on recent work (López et al. Phys. Rev. Lett. 99, 188701 (2007)) that addresses the effect of limiting the effective path length of communication of some agent such as a pathogen, we can improve current estimates of epidemic thresholds in the population. Additionally, by considering the removal of individuals from the contact network, we can also determine more realistically the level of intervention needed in order to prevent an epidemic.

Theme IV: Models with reinfection (FGC-IGC, FFCUL, TAU)

Task 11 Formulate measures of transmission in the presence of reinfection: A keystone concept in

epidemiology is the basic reproduction number R_0 which is defined as the expected number of secondary infections generated by a single infected individual in a completely susceptible population. This concept is central to public health management, as it indicates R_0 =1 as the target for both disease eradication and re-emergence. After having demonstrated its value in the eradication of smallpox and in the management of measles mumps and rubella, the knowledge of R_0 appears useless when reinfection plays a significant role. Recurrent infections are in urgent need of meaningful measures of transmission that can indicate useful targets for public health interventions. Such measures are tightly linked to the specific mechanism of reinfection and will be formulated through simple mathematical models.

Task 12 Parameter estimation: Influenza will be used as a case study for the validation of the different theoretical developments in this work package. Model evaluation will be carried out with data from seasonal influenza, as generated in Influenzanet (WP5) as well as established national influenza surveillance systems. The new model structures change parameter estimation schemes, and can be tested explicitly on the incoming data, in order to evaluate the prediction quality of the models. On the basis of models developed in this work package, we will develop new tools for estimating the onset of the influenza season which is in general highly variable. These estimates, obtained through stochastic modelling processes, will be more robust than the commonly used threshold conditions applied in different countries with their varying case definitions. By combining the different theoretical developments and parameter estimation methods ,we expect to make significant advances to the understanding of what components must be included in early warning systems for infectious diseases. These features will be further elaborated in WP2 through computational approaches. The modelling structure will be stochastic models (Master equation) explicit in contact structure, by including adjacency matrices in the infection terms (see Stollenwerk, Martins, Pinto, Physics Letters, 2007), from which approximation schemes can be derived.

Deliverables (brief description) and month of delivery

1.1 Analysis of dynamics on clustered contact networks (month 12).
1.2 Practical transmission measures in the presence of reinfection (month 24).
1.3 Models of disease transmission under seasonality and other external drivers (month 36).
1.4 Models of spread, impact and evolution of vector-borne pathogens, including the demography and ecology of host species (month 36).
1.5 Model parameterization, simulation, prediction and quantification of uncertainly (month 48).

WP 2 – Spatially structured models and human mobility

Work package number	2		**Start date or starting event:**	Month 1		
Work package title	**Spatially structured models and human mobility**					
Activity type[12]	RTD					
Participant number	**4**	1	2	3	9	10
Participant short name	**MPG**	ISI	FGC-IGC	TAU	BIU	FBK
Person-months per beneficiary	102	24	56	46	25	13.5

Objectives

[12] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

Two of the most challenging aspects of complexity in the epidemiological context are the structure of interacting populations on many magnitude and spatial scales beyond and within international, interregional, intercultural and linguistic boundaries and their effective interaction by means of multi-length scale transportation and mobility networks. On the other hand, the development of an epidemic forecast structure crucially depends on the ability to quantify the topological features of human mobility networks, the development of theoretical frameworks that provide order parameters to classify them, extract universal features and reveal differences on an international, national and regional level. These are the key objectives of this WP. A first key objective of WP2 is the development of systematic approaches that can identify and quantify modularity in spatially structured and heterogeneous meta-populations and contact networks. One of the key questions we address is: “How much geography, cultural diversity and spatial variability is encoded in the topology of mobility networks?” In contrast to the arbitrary use of, for instance communities provided by political units (countries, regions, federal states and counties) we will employ community structure identification algorithms to identify the effective community structure in multi-scale mobility networks. This will permit a quantitative systematic definition of effective modules in meta-populations, provide an operational definition of sub-populations and reveal the magnitude of boundaries between them.

A second objective of WP2 is the investigation of human interactions in a network-network duality ansatz. The theme on contact networks of WP1 is intimately related to the aim of WP2. The statistical properties of contact networks is strongly influenced by the way individuals behave as agents in a spatially structured meta-population. Contemporary research on disease dynamics has so far not succeeded in merging these two aspects. We anticipate to bridge this gap in a network-network duality framework. The key goal is to understand the reciprocal impact of social networks and mobility networks. To what extent are contact networks determined by mobility networks and vice-versa? In this approach we plan to develop mathematical tools and theoretical frameworks that permit the development of models in which social contact networks and mobility networks are modeled simultaneously. A solid theory for this will also permit the aid the identification of the underlying meta-population based on measurements of contact patterns. A third objective is the use of the above results to advance the understanding of the prediction quality offered by large scale computational approaches and realistic agent based models. Their sensitivity to initial conditions, parameter fitting or incomplete information can be tested by relying on tools and concepts borrowed from complex systems theory and applied in the context provided by the study on the metapopulation structure offered by the WP2.

Description of work

Theme I: Structure of human mobility networks (MPG,BIU,TAU, ISI)

Task 1 The statistical properties of multi-length scale European mobility networks: No comprehensive study exists of traffic networks incorporating all spatial scales. This would require collecting and compiling data for these means of transportation into a comprehensive multi-scale network, a particularly difficult task that has not been established for modelling frameworks for infectious disease dynamics. Whereas central statistical features (degree distributions, centrality features, node inhomogeneities, etc.) of air transportation networks have been studied in detail, it remains unclear whether these properties remain unchanged in traffic networks that comprise all other means of transportation. How do these properties depend on the length scale? Are they universal? In what way do they change as a function of length scale? We propose the analysis and characterization of a large number of data source (census, airlines, commuting patterns).As well, we propose a novel approach to this problem that will use the concept of proxy mobility networks. This approach is based on the idea that humans tend to transport items whenever they travel, and for specific items large datasets are available. We plan to evaluate two different datasets derived from similar internet data: 1.) Eurobilltracker.com (analogous to wheresgeorge.com) 2.) Geocaching.com, a modern, international GPS treasure hunt in which trackable items are transported by travelling humans from place to place and 3.) bookcrossing.com an internet administered game of similar nature. All of these proxy datasets contain a massive number of records and can be used to estimate statistical properties of particular aspects of human mobility with very high spatio-temporal accuracy and across international boundaries.

Task 2 Multi-scale Community structure and Effective geographic boundaries in Europe. A key question for understanding disease dynamics in spatially structured meta-populations is the identification of communities of all spatial scales and boundaries between them. We anticipate using regular traffic and census data along

with the above proxy networks of human mobility to identify and understand the effective community structure in Europe based on interactions across distance. We plan to devise new and apply existing graph-cutting algorithms for finding maximum modularity partitionings of multi length scale mobility networks. A number of important questions that arise in this context: Are large scale communities in the 21st century spatially compact or not? For instance large European metropolitan areas such as Paris, London and Berlin could belong to the same effective community due to their significant coupling strength. To what extent do effective boundaries provided by these algorithms correlate with existing political boundaries, linguistic boundaries and geographic features such as rivers and mountain ranges?

Task 3 Effects of spatial embedding on contact network structure: Unlike other complex networks human mobility networks are embedded in a two-dimensional space, origin and destination locations possess coordinates and the notion of geographic distance not only provides additional information but imposes constraints by the spatial embedding that can lead to significant consequences in structured models of mobility, particularly at certain scales of the problem. Therefore, such constraints need to be understood both in theory, as well as in how they impact epidemic spread and intervention strategies. We will consider rules of human mobility and connection when spatial embedding is present, in order to evaluate the unknown rules of human contact relevant to disease propagation. This kind of analysis can then be matched to other scales of the problem such as air-travel, shipping and supply networks, etc. which inject additional effects and scales to the contact structure of the population. This work complements part of WP1 because it gives yet another aspect that is relevant to the construction of precise contact networks to study epidemics. Also, aspects associated with WP1 relating to effects of limited path need to be considered, where in this case, the limited path effect is related to human mobility (as opposed to pathogen seasonality or mutation as in WP1).

Task 4 Immunization strategies for spatially embedded networks. In WP1, the problem of immunization is treated for general networks. When the particulars of networks generated inside some spatial embedding are considered, immunization strategies should be adjusted accordingly. Therefore, we will consider alternative methods of immunization specifically tailored to these network properties. These spatially embedded networks may also require immunization approaches that are optimized to the case of partial or full information about the network.

Theme II: Network-Network duality: The interplay of human mobility and social contact networks (MPG,TAU, BIU)

Task 5 Network-Network Duality in Heterogeneous Metapopulation and Contact Patterns I. The basic question here is: what is the imprint of the transportation meta-population structure (nodes=populations, links=traffic) on the cities subpopulations which have their predefined social contact networks (nodes=people, links=interactions)? Apart from large-scale simulation models, as yet there is no way to gain deeper insights into important questions of this nature. Based on observed features of real-world transportation infrastructures and of dynamic contact patterns obtained from embedded sensor technologies (see the Bluetooth experiments in WP5), we propose a mathematical framework for analysing "network-network" duality scenarios allowing both for the social interaction network within subpopulations together with the transportation network between subpopulations. Taking this further, consider a population with, say, N=1 million individuals who interact through their social network structure. The large population can be split into a meta-population of 1000 villages each having N=1000 individuals. With no inter-village interactions, this would result in 1000 smaller social networks having similar statistical properties as the original large population, only with higher fluctuations because the villages are smaller in size. Switching on interactions between villages by means of travelling, the nature of the entire social network of the meta-population will change. The model we propose will be able to predict the statistical imprint of the heterogeneous meta-population on the social network that it embeds. More than that, the model will allow determination of precise conditions on how both the transport network and the social network will constrain large-scale persistence of an emerging disease in the set of cities. Thus for the first time, the effects of heterogeneity in contact networks and transport networks will be modeled in a unified framework. It will permit mathematical investigation of important epidemiological scenarios, such as super-spreading individuals in city-networks that have unusually large traffic hubs.

Task 6 Network-Network Duality in Heterogeneous Metapopulation and Contact Patterns II The correct formulation of a mapping that takes a social contact network of individuals into an effective network of

meta-populations needs to be able to fit observational data. Conceptually, this is equivalent to stating that any meta-population network has to be measurable from data, and should be useful for the fine tuning and testing of the theoretical framework proposed in WP2 Task 5. Analyzing high resolution spatiotemporal data currently available for certain European countries (e.g. respiratory diseases encoded in Hospital Episode Statistics of the UK National Health services), one can directly detect meta-populations by their signal signature, i.e., places which are displaying diseases in a synchronized way would represent meta-population nodes, and other places desynchronized from the first would represent independent nodes. Linkage between nodes can be tested over long periods to time in which multiple epidemic periods can be studied seeking persistent patterns of disease propagation. Once a propagation pattern has been well characterized, linkage between meta-populations can be introduced, creating the large scale, effective epidemic networks of the population. The detection of meaningful signals to construct these networks can be done through an array of methods such as Fourier analysis, Principle mode decomposition, etc. The results of our analysis and its matching to WP2 Task 5 would represent the strongest tests of the method and would consolidate the network-network duality method.

Theme III: Dynamics on heterogeneous networks: theoretical foundations and high performance agent based simulation (ISI, MPG, FGC-IGC, FBK, TAU)

Task 7 Agent Based and multi-scale models: basic properties on complex networks and meta-population paradigms: We plan to take advantage of the analogies of spatially extended and agent based models with multi-particle systems and reaction-diffusion processes, to use techniques developed in the study of critical phenomena and systems with diverging fluctuations. These techniques are aimed at the analysis of systems composed of a large number of interacting particles and will provide the basic theory in simple multi-scale epidemic models with complex interaction network topologies. The questions we plan to address include the study of the epidemic threshold, typical time scales of these systems, the effect of complex network topologies characterized by large heterogeneities on the disease evolution and the role of correlations at various distinct levels. This will provide a framework for relating the microscopic properties of agent dynamics to the overall macroscopic behavior of the model. A key focus will be the properties of epidemic thresholds as the detailed evaluation of the variation of this threshold with respect to different mobility schemes that is crucial in order to achieve a basic understanding of the central factors controlling the onset of global outbreaks.

Task 8 Agent based simulations in multi-scale and multi-level Network-Network systems. In agent based spatially extended models individuals move between diverse environments where they have contacts (households, schools, workplaces, hospitals, etc.). Random contacts in the population among (and within) the local communities can be modeled by assuming that all individuals exhibit identical travelling rates that are estimated from available travel data. However, individuals typically exhibit highly variable travelling rates (e.g. frequent travelers) and this may affect the overall rate of spread of an epidemic giving rise to possible super-spreading phenomena. We will investigate the implications of variable travelling rates in spatially entended epidemiological contexts and extract effects on key epidemiological parameters and phenomena such as fade-out and extinction probabilities, spatio-temporal pattern statistics and synchronization effects.

Task 9 Complexity and predictability in computational epidemiology: A meaningful large scale computational approach to epidemic modelling requires an thorough understanding of the predictive power of complex epidemiological models. This implies a basic understanding of the predictive time scale as a function of information available on the system and its initial conditions. Whereas the analysis of chaotic properties in basic epidemic models has a long tradition, computational epidemiology faces issues related to the large scale of the extended dynamical systems and its complex properties for the first time. We plan to assess issues concerning the complexity and predictability of epidemic spreading patterns resulting from multi-scale and agent based computational models by integrating techniques used in information theory and statistical physics. Tools such as damage spreading, traditionally used in biology and in physics, will be applied to quantify the predictability of agent based models whose large scale analysis differs from the usual ones used in continuous dynamical systems.

Deliverables
2.1 Implementation of multi-scale proxies networks for human mobility networks from online data-sources: www.geocaching.com, www.bookcrossing.com, www.wheresgeorge.com, www.eurobilltracker.com. (month 12). 2.2 Theoretical foundation and mathematical description of network-network systems, i.e. spatially embedded contact networks and empirical validation by case study of respiratory diseases in the UK (month 24) 2.3 Development of theory and stability analysis for limited path multiscale transportation networks: (month 36): Networks that take into account effective multiple length scales of transportation, and their couplings. Rules for the link strengths between contacts that take into account the multiscale problem. 2.4 Spatially embedded networks (month 36): Specific rules for contact in the context of spatial embedding. Properties of the networks subjected to such spatial embedding constraints. 2.5 The development of order parameters and quantitative indicators for predictability in complex multi-scale epidemiological dynamical systems. (month 48).

WP 3 – Information platform

Work package number	3		**Start date or starting event:**		Month 1			
Work package title	**Information platform**							
Activity type[13]	RTD							
Participant number	**12**	1	2	3	4	5	9	10
Participant short name	**FFCUL**	ISI	FGC-IGC	TAU	MPG	AIBV	BIU	FBK
Person-months beneficiary	82	60	4	8	42	4	11	6

Objectives
The overall objective of an epidemic forecast infrastructure is ultimately the support of modelling approaches addressing the required complexity/realism requirements for explaining and predicting the spatio-temporal dynamics of infectious disease propagation at the global scale (with a focus on Europe). Here we develope an information platform to mediate access to distributed collections of public health data, offering an easy and safe way to share data for those data providers who want to collaborate with epidemiological modellers. Researchers will use this platform in multiple ways: i) as catalogue of data sources containing the metadata describing existing databases; ii) as a forum to publish information about their own data, seeking modellers to collaborate with, and/or to seek sources of data that could be of interest to their epidemiological modelling efforts; and finally, iii) as the host of mediating software that can automatically process queries for epidemiological data available from the information sources connected to the platform. Once these epidemiological data are properly characterised, work will proceed towards developing a common meta-model for querying data of interest for epidemiological modelling architecture using state-of-the-art semantic-web/grid technologies. This platform is envisioned to mediate access to distributed collections of public health data, offering an easy and safe way to share data for those data providers who want to collaborate with epidemiological modellers through a publicly available Web interface. Drawing on the successful web2.0 interaction designs that drive popular file and content sharing community sites like Flickr (http://flickr.com/), YouTube

[13] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

(http://youtube.com/), or Wikipedia (http://wikipedia.org/), the Epidemic Marketplace Platform will go beyond the concept of data repository, relying on the active contribution of web users. However, instead of sharing images, movies, or encyclopaedia entries, scholars will use the application to share datasets, algorithms, visualizations, and other items relevant to the study of epidemics. An inspiring project is “Many Eyes”, an experiment by IBM Research on a collaborative web platform for sharing datasets and their visualizations (http://services.alphaworks.ibm.com/manyeyes/).

Modelling approaches can use the platform to find out who has required data. As the data are not stored centrally, we avoid privacy and security concerns that would limit both the data providers and the modellers searching for collaborations. Once potential collaborators have identified each other, data and modelling expertise sharing can be discussed and the collaborators can opt for either sharing the data directly on the basis of trust, or agreeing on controlled sharing, respecting privacy, ethical rules and access restrictions required by the information providers. The development of this platform for metadata exchange will make it a useful resource enabling collaborators to easily find each other, and define mutual voluntary agreements for sharing their data. These agreements will be chosen from pre-established templates setting terms & conditions.

When considering the objective of hosting mediating software that can automatically process queries for epidemiological data available from the information sources connected to the platform, some issues will have to be tackled directly by the platform itself. For instance, to deal with privacy and restricted access-control rules, we intend to adopt and further develop state-of-the-art grid technologies related to the authentication and authorization processes, together with anonymisation and pseudo-anonymisation techniques.

Conventional epidemiology of infectious disease demands extensive collections of data. The range of data required will vary depending on the type of study, but certain elements are required: a degree of confidence in the data is essential, so its *provenance* has to be assured and the standards of clinical practice under which it was obtained have meet pre-established requirements. Despite the fact that the data may be gathered under different clinical regimes, it must still be possible to establish their semantic equivalence, to ensure that aggregation or comparison of datasets is legitimate.

One of the most critical processes for integration of a set of heterogeneous data sources is the curation of the available data. Often database contents are inconsistent or have information that does not follow a standard nomenclature or filling process. This entails the loss of information, and reduces user confidence in the system. Therefore, collaborative epidemiological data curation is another research issue related to this proposal. This issue can be handled, for instance, through tracking data provenance and normalization of the nomenclature used by different sources using established ontologies when integrated queries are processed or new metadata is fed into the system.

Access to Geo-referenced data is also very important in epidemiologic studies. It is important to provide access to geo-referenced data for spatiotemporal related analysis through integrated queries. In order to do so, the epidemiological meta-model to be developed should address the particularities related to geo-referenced data.

The platform will be implemented on a grid platform based on standards defined by the Open Grid Forum, the Globus Alliance and the OASIS consortium.

Description of work

Task 1 (FFCUL, ISI, FBK, BIU, MPG, FGC-IGC, AIBV): Data collection

Realistic simulations of epidemic processes crucially depend on the availability of datasets describing human behaviour and pathogen-host interactions. Datasets include population movement data, social and behavioural data, health related data, geographic data, detailed geo-temporal epidemic incidence and immunization data, pathogen evolution and multi-strains circulation data. Data can come from a variety of different sources, including hospital records, country statistics, Web content, and others. It can range from a global scale, such as the worldwide air transportation infrastructure, down to the detailed description of individual activities at a minute-by-minute scale. This task will create a catalogue of databases of epidemiological data across Europe, with extensive meta-data describing the main characteristics of the available information sources. This catalogue will be integrated with a collaborative platform that will be setup for online discussion and exchange of meta-data among the participants.

Task 2 (FFCUL, IGC, ISI): Meta-model design

While some of the previously mentioned datasets are freely available on the Web (e.g. WHO Global Health

Atlas, Eurostat), they are often scattered in different repositories, cover partial regions of the world and come in different formats, according to different standards and classifications. The project envisions a unified and integrated approach for the management of these resources, with the design and implementation of an Epidemic Marketplace Platform, publicly available on the web. The platform supports the sharing and management of epidemic datasets and resources as well as their rating, annotation, and selection. It is an on-line social networking site that will serve researchers, practitioners, and educators all over the world to foster a virtual community for epidemic research. It will support the exchange of resources as well as user interactions. Based on a Web2.0 approach, users will become active participants, sharing information and data, and collaborating online, rather than being satisfied with a passive information consumer/viewer role.
We envision proposing a simple reference format which will facilitate the navigation and use of the datasets. Each dataset will come with a metadata file, signalling the date of submission, the last update, the source of the dataset, a basic profile (e.g., transportation network – Origin-Destination matrix), and a more thorough description of the dataset and the classification used. The Marketplace will support flexible and intuitive tools for navigation and selection of resources. Standard classifications as well as tagging systems proposed by users will be supported.

Task 3 (FFCUL, ISI): Epidemic Marketplace Platform
This task will implement a platform based on the integration of grid technology and publicly available services and software on the web to support the sharing and management of epidemic datasets and resources as well as their rating, annotation, and selection. The Epidemic Marketplace Platform will be an on-line social networking site that will serve researchers, practitioners, and educators all over the world to foster a virtual community for epidemic research. It will support the exchange of resources as well as user interactions. Based on some of the Web2.0 characteristics, users will become active participants, generating information and providing data for sharing, and collaborating online, rather than being satisfied with a passive information consumer/viewer role. More specifically, researchers can use and contribute to the Marketplace in several different ways. They can: (1) use it as a catalogue of data sources containing the metadata describing existing databases; (2) view, download, tag, and comment on the available resources; (3) provide compliant datasets and relevant information; (4) use it as a forum where to publish information about their own data, seek modellers to collaborate with, share and distribute their new findings.

Task 4 (FFCUL): Evaluation and monitoring of the use of the catalogue and collaboration services.
This task involves the monitoring of epidemiological data exchanges performed through the mediating services platform. The evaluation will assess not only the coverage of the catalogued resources, but the users' satisfaction with the user interface and integrated collaborative tools made available through the epidemiological marketplace platform. More importantly, the analysis of the collected datasets and their annotations and usage will provide a rich environment for deriving an epidemiology ontology, which will help further on the integration and communication among the community of epidemiologists.

Deliverables
3.1 Report - Meta-model initial specification , catalogue of relevant data, platform requirements (month 8)
3.2 Prototype of the Epidemic Marketplace Platform with initial an initial set of epidemiological databases integrated available to project participants (month 12).
3.3 Public release of the Epidemic Marketplace Platform (month 20).
3.4 Report for the Epidemic Marketplace Platform after release, describing changes and new implemented features, new data sources integrated with the platform, results of user surveys and usage statistics (month 36).
3.5 Report – Epidemic data ontology (month 36)
3.6 Report – Final specification of the Epidemic Marketplace Platform and evaluation results (month 48).

WP 4 – Epidemic Modelling Platform

Work package number	4	Start date or starting event:		Month 1		
Work package title	**Epidemic Modelling Platform**					
Activity type[14]	RTD					
Participant number	**1**	2	3	4	9	10	12
Participant short name	**ISI**	FGC-IGC	TAU	MPG	BIU	FBK	FFCUL
Person-months per beneficiary	72	12	52	42	30	25	19

Objectives

Key to the development of an epidemic forecast infrastructure at the European level is a computational platform that can provide the access to the state-of-the-art modelling approaches to perform data-driven simulations of epidemic outbreaks. The project foresees the design and implementation of an *Epidemic Modelling Platform*, made available to a wide range of users through the Web. Modelling algorithms developed in WP1 and WP2 will be interfaced with the relevant data available from the information sources listed in the Epidemic Marketplace Platform developed in WP3, with the aim of providing a simulation platform for several distinct infectious diseases and granularity scales of the system. Newly developed visualization techniques will be embedded in the platform to provide access and understanding of the simulation results. The aim of this data-driven computational resource will be manifold: it will allow researchers to simulate epidemics by explicitly including the complexity of the real world in order to achieve a better understanding of the disease dynamics; it will allow public health workers to train on real-world epidemic outbreaks simulated in a computer; it will provide policy makers with risk assessment scenario analysis to enable appropriate decisions at the management level for a critical epidemic situation; it will allow a wide range of users to access technologies and expertise of high quality in the field of realistic simulations of epidemic processes; it will enable students in a variety of different fields to get familiar with the research in this field, understanding the advantages of this multi-disciplinary approach.

Description of work

<u>Task 1 (ISI, FBK, BIU, MPG): Data integration into modelling algorithms</u> Epidemic modelling involves a multitude of datasets and algorithms that need to be combined in appropriate ways. Computational models take in parameter values (e.g., disease parameter values, population movement data, etc.) and substrate data (e.g., map of Europe) to simulate epidemic processes in a given framework. Real world data (e.g. historical epidemics) and simulation results are then analyzed and compared in order to further our understanding of the spreading process, identify key mechanisms, develop and test intervention strategies, identify patterns, analyze scenarios, etc. Datasets of different kinds will need to be interfaced with the algorithms for different purposes to provide:

- Fundamental ingredient information as an input of the modelling approach (e.g. transportation networks as coupling terms of multi-scale approaches);
- The benchmark for the simulation results (e.g. historical epidemics data for the analysis of a specific case-study or for a model validation);
- The appropriate frame of reference for the representation of the simulation results (e.g. geographical data to be synchronized with the simulation output to provide a visual representation of the spreading evolution on a map).

The relevant data will be made available directly on the Epidemic Marketplace Platform developed in WP3 or from sources collected therein. Multi-scale and agent-based models designed and analyzed in WP2 will be

[14] Please indicate <u>one</u> activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

interfaced with real-world extensive data.

Task 2 (ISI, MPG, FFCUL, FBK): Data and simulation results visualization
Understanding the spatial spread of an infectious disease is crucially related to our ability to visualize data and results in relation to the underlying geography. Maps are used in public health with the aim of identifying patterns, characterizing behaviours, predicting outcomes, informing and empowering health related decision making. We plan to develop visualization techniques that are specifically custom-designed for use in public health, leveraging on Geographic Information Systems (GIS), powerful automated systems for the capture, analysis and display of spatial data. The geographic spread of diseases can be represented on choropleth maps that examine disease incidence at a given level of spatial resolution (municipality, state, country, region, continent, worldwide). Map layers can be vertically overlayed and integrated to provide, for example, insight into the correlations of the observed patterns with infrastructures. Map distortions can provide an additional perspective on the patterns linking health data with environmental and socio-economic data. Innovative visualization techniques will be developed that will cope with the multiple levels of representation considered in the models. The visualization of the dynamical behaviour of large-scale systems represents both a theoretical and technical challenge that deals with producing easily readable and meaningful representations of massive amount of interlinked time-dependent information. We plan to merge GIS tools with network visualization techniques to shape new methods to visualize the geotemporal spread of infectious diseases. Georeferenced contour plots can be mapped in order to visualize isolines connecting points in space where a given feature (e.g. epidemic activity) assumes a same particular value. Fronts of invasion and local epidemic waves can be shown with dasymetric mapping techniques in contrast to the patchy and non-diffusive behaviours resulting from long range transportation. This task will also produce different kinds of mashups as web applications that vertically integrate layers of maps with other sources of relevant information available on the web. In particular, this integrated tool will make use of the data and metadata available in the Epidemic Marketplace Platform (see WP3) to display e.g. transportation infrastructures, population distribution, hospital locations, incidence data, previous epidemic season data, etc. in a multi-layer fashion with zoom-in and zoom-out features on top of Google API maps.
A variety of visualization techniques will be seamlessly integrated into the Epidemic Modelling Platform workflow (see following task) for easy-to-use access by public health practitioners.

Task 3 (ISI, FBK): Epidemic Modelling Platform
This task will design and implement a platform for the computational modelling of infectious disease spread. Relying on the epidemic modelling approaches developed and assessed in WP1 and WP2, the Epidemic Modelling Platform will integrate real-data (Task 1) and visualization techniques (Task 2) to perform simulations and provide access to the state-of-the-art computational modelling to a wide audience of both experts and non-experts. The aim is to provide a flexible and user-friendly tool for the simulation of a case study, test and validation of specific assumption on the spread of a disease, understanding of observed epidemic patterns, study of the effectiveness and results of different intervention strategies, analysis of risk through model scenarios, forecasts of newly emerging infectious diseases. The algorithms will be coded in C/C++ to ensure greater flexibility and maintainability as well as high speed in large-scale simulations. They will be made freely accessible on the Epidemic Modelling Platform via the Web to be run by any user. No programming knowledge or computational expertise will be required to use the Platform. Modelling approaches will be associated with corresponding documentation files, which will report detailed information on the algorithms, implementation details, notations and conceptualization adopted, references, hints for the user, instructions on how to use it, applications, suggested actions, and examples. Users will be prompted to choose from a series of built-in approaches through menus in a recommendation system fashion that will help them identify the most suitable algorithms for their specific aim/problem. This recommendation system integrated in a series of wizard-like panels will be extremely helpful for the interaction of a non-expert user with the Platform, allowing the use of complex computational tools by people who do not necessarily have this kind of expertise.

Task 4 (ISI, FBK, FGC-IGC, BIU, TAU): Data-driven simulations for case studies analysis and epidemic forecasts: national scale The Modelling Platform will be used for large-scale data-driven realistic simulations of the spread of infectious diseases at different scales. This task will focus on the national scale. Building on the expertise of the FBK partners, we plan to extend agent based modelling approaches (now developed for Italy) to other participating countries, taking advantage of socio-demographic data collected in WP3 and of

the users' contributions to the Epidemic Marketplace Platform. These approaches will be for example used in the simulation of seasonal influenza as a case study at the national level. Simulation results will be checked against the surveillance data collected through innovative ICT tools in WP4, with the aim of understanding short and long range spatial spread, characterizing annual epidemic waves and identifying key elements that determine their geotemporal evolution. Results from different countries will be compared to determine country-specific scenarios that will help in the preparedness planning, public health decision making, resource allocations, etc. On a micro-scale, detailed hospital records available in some participating countries (e.g. UK, Israel) will be used to test the modelling system on other diseases as well, addressing multi-scale analysis bridging resolution scales (whose methods and effects have been addressed in WP2), investigating correlations between population movements and disease spread, exploring possible correlations in the evolution of different diseases. Side by side runs in which model epidemics under a specific set of input parameters can be compared to the real case from the national level data would allow for direct, interactive adjustment of parameters for individual diseases, years of data, and specific strains of a pathogen. Even special circumstances, such as suspension of transportation services in the past can be studied and compared to the real data.

<u>Task 5 (ISI, FBK): Data-driven simulations for case studies analysis and epidemic forecasts: European and worldwide scale</u> Alongside the simulations at the national level (Task 4), the project will address larger scale simulations, based on metapopulation approaches – informed by agent based models at local community scale (see insights from Task 8 of WP2) – at the European scale and at the worldwide level. Simulations of seasonal influenza in Europe will further improve our understanding of the epidemic progression. Surveillance data collected from the European Influenza Surveillance System will be used as a benchmark for the case study. Impacts of multi-scale community structure and effective geographic boundaries in Europe (addressed from a theoretical point of view in WP2) will be studied and tested in the simulations. The computational platform will also be used for the study of different infectious diseases than influenza and to address problems related to bioterrorism attacks, preparedness plans, management and optimization in the allocation of health related resources (e.g. drugs and health workers) in a wider European perspective. Informed by the results achieved in WP2, and based on trans-national typical individual behaviours (e.g. travelling behaviour), this task will also test individually targeted intervention measures and their effect in the mitigation of an epidemic outbreak in Europe.

Deliverables

4.1 Static single layer visualization techniques (choropleth maps, distortions, dasymetric maps) and simple mashups (month 12).
4.2 Prototype modelling suite of the Epidemic Modelling Platform programmed including contact patterns and population mobility as emerging from WP1 and WP2, with documentation (month 20).
4.3 Public release of the Epidemic Modelling Platform (month 32).
4.4 Report for the Epidemic Modelling Platform after release, describing changes and new implemented features, new visualizations and modelling algorithms integrated with the platform, results of user surveys and usage statistics (month 40).
4.5 Application of Epidemic Modelling Platform to seasonal influenza modelling in (i) participating countries; (ii) Europe; (iii) worldwide. Comparison with influenza surveillance data and harmonization of European countries preparedness plans on early and efficient responses to health emergencies (month 48).
4.6 Report – Final specification of the Epidemic Modelling Platform, evaluation results, academic papers (month 48).

WP 5 – ICT monitoring and reporting system

Work package number	5	**Start date or starting event:**		Month 1			
Work package title	**ICT monitoring and reporting system**						
Activity type[15]	RTD						
Participant number	**5**	1	2	11	6	8	
Participant short name	**AIBV**	ISI	FGC-IGC	CREATE-NET	LSHTM	KULeuven	
Person-months per beneficiary	60	36	88	36	25.5	24	

Objectives

In 2003 a successful pilot project proposed novel internet-based approaches to monitor influenza-like illness (ILI) with direct participation of volunteers in the Netherlands and Belgium: Grote Griepmeting (www.degrotegriepmeting.nl/) or Great Influenza Survey. The system is conceived to inform and educate the population about the disease and to collect real-time information on the distribution of ILI through web-services. Graphic representation, processing and analysis of data on the progression of the disease, is provided in real time. Following the Dutch example, the FGC-IGC started Gripenet as internet-based monitoring system (IMS) in Portugal in 2005: www.gripenet.pt/. The two projects in three countries are highly successful, as they turn out to be of high value in monitoring, epidemiological analysis and in recruiting respondents, with 55.000 accounts in Belgium and the Netherlands and 5.000 in Portugal. In 2008 the ISI foundation started www.influweb.it as a pilot project in Italy. In many other European countries there is serious interest to implement a similar internet monitoring system. A large European-wide deployment of such a novel monitoring infrastructure would provide crucial advantage to modelers for real-time data feed to forecast algorithms. For reasons of geographical unity and existing contacts with professional organizations in Sweden, UK, France, Spain and Germany we propose to enhance introduction of IMS in these five countries. The first year is a pilot year including determination of a ‘golden standard’ set of ILI symptoms, database infrastructure preparation, internet database design, translation of documents and testing. In the subsequent flu seasons of 2010-2011 and onwards, we will follow a gradual approach in introducing IMS first by two countries and later by one country at the time. Despite the work on the IMS platform consider an a common template web platform and database structure, the implementation of the IMS in each country represents a separate scientific challenges and research problems. Each country has different population stratification and geographical distribution. The IMS has to take into account these differences and design specific mapping/representation solutions as well as finding the optimal granularity for the data acquisition and statistical sampling. This has to be devised in conformity with administrative divisions and historical records and consider the national mobility patterns. Communication and recruitment strategies will need to be devised to target the different populations of the ‘new’ IMS countries, each characterized by different habits (e.g. different diffusion of the Internet use in the population, different access to national media, different structures and organizations of school to contact for educational projects, etc.) and therefore reactions and feedbacks to the implemented strategies.

Therefore the *first* objective of this work package is *to enhance the portability of this interactive and efficient system and to extend its implementation into five new countries: Sweden, UK, France, Spain and Germany*.

It is a well known fact that in many countries a fair share of the population does not have access to internet services. This applies particularly to elderly people and people living in rural areas. In order to ensure that monitoring of health conditions can also be carried out for such parts of the population, mobile phones could

[15] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

be used as enabling access technology. This is rooted in the observation that mobile phone services provide almost ubiquitous coverage and that the diffusion of mobile phones in the population is extremely large, covering also those people who do not have access to/are not familiar with web interfaces. Using mobile phones would therefore mean two channels of communication and data collection through ICT. A *second* objective therefore is *to extend the web-based interfaces for collecting data on people's health status by using mobile phones as target devices*.

The simplicity and success of IMS for influenza motivates the extension of the concept and methodologies to other infectious and allergic diseases. Given the commonality of both respiratory and diarrhoeal diseases we will primarily develop extensions of internet-monitoring system in this context. A *third* objective of this work package is *to design and implement schemes to monitor respiratory allergies and common diarrhoeal infections with the direct participation of the population*. Strategies to improve the awareness of the population for risk environments and behaviours will also be contemplated.

Finally, we aim to extend IMS with questionnaires for our volunteers in order to gather enhanced surveillance and behavioural data for the purpose of improving dynamic mathematical models of influenza transmission. This extended information would enable the accurate parameterisation of models for both seasonal and pandemic influenza and could be readily adapted to cope with other newly emerging or re-emerging pathogens.A *fourth* objective of this WP is *the extension of IMS with data on contact patterns.* It is intended that by linking individuals' self-reported contact patterns, and the development of disease, quantitative information will be derived on the risk of infection according to individual-level and network level characteristics.

WP5 activities strongly contribute to the global project objectives. IMS and its internet database will provide the data that will be used by other parts of the project.

Description of work

Task 1 (KULeuven, AIBV): Design of a 'golden standard', a set of ILI symptoms to be applied in all participating countries. This requires frequent (e-mail) contacts among epidemiologists from the nine IMS countries (NL, B, P and I and S, UK, F, S, and D). The KULeuven team coordinates this task. This Task is crucial for the project's aim of gathering cross-country surveillance data that do not suffer from national-related biases and methods. Epidemiologic research will be translated into an appropriate survey that best describes the need of different countries in the data collection method regarding the population (e.g. which demographic/stratification data to ask the user in order to match existing national statistics databases) and the infectious disease (e.g. related to different habits and/or law regulations for the absence from work).

Task 2 (AIBV): Design and implementation of a database infrastructure for IMS in Sweden, France, Spain, UK and Germany, including the following subtasks:
- the joint preparation of a single centralized database:
- design of templates in five (new) local versions;

Database contents of local IMS will be designed to be consistent and have information that follow a standard nomenclature. Surveillance data gathered locally in each participating country will be collected in a centralized database that will provide an easy-to-access, reliable and extensive source of epidemiological data. The design and implementation of the single database infrastructure is extremely important to allow each research team to have an easy access to the surveillance data to be used in WP4 for simulation comparison, not hampered by problems related to different standards, different languages, different accesses to computational and storage facilities across country borders. In this sense, the design of the new IMS templates will be crucial: the existing IMS infrastructures have been designed with a strongly regional target, while the devising and implementation of cross-country templates is fundamental to build an integrated and collaborative platform aimed at gathering country-independent surveillance data.

Task 3 (AIBV, ISI, KULeuven, FGC-IGC): Design and implementation of an internet database with English language documents on influenza, flu information packages for schools, 'flu games', press information, and, of course, all the scientific information required for translation into Swedish, French, Spanish and German.

This internet database – "Influenzanet" – is linked by ISI to the Epidemic Marketplace Platform of WP3.
Subtasks:

Task 4 (AIBV, KULeuven, FGC-IGC): Local coordination in the 'old' IMS countries, Netherlands, Belgium, Portugal, Italy and in the 'new' IMS countries: Sweden, UK, France, Spain and Germany. This includes: preparing and implementing the IMS database in local version in the first flu season, 2009-2010. This is a rehearsal in the 'old' IMS countries and a pilot phase for the 'new' countries. AI BV will coordinate this task with KULeven and IGC assistance and consultancy. The implementation in the new countries will leverage on the experience gained in the 'old' IMS countries, where the IMS was targeted to the country local situation/habit/environment. With the development of a golden standard of case definitions and survey schemes (see Task 1), the implementation of a unique database infrastructure where to collect all data coming from the different countries (see Task 2), and the availability of related documentation and information pages in different languages (obtained through Task 3), we aim to build a concretely portable system for surveillance that can be more easily exported and implemented in different countries. However, many issues still need to be considered in the unique standard approach. Each system will need to be based on local country data, as e.g. demographic data, age stratification data, and geographic data at different resolution scales. Data will need to be collected, analyzed, and synchronized. Each system will need to deal with the local privacy regulations to ensure privacy protection of the personal data submitted by each user. Problems of data handling and visualization of results at different scale resolution will need to be addressed and to conform to the local scenario: e.g. the choice between administrative regions and postal codes, conformity of the choice made with the national privacy regulations, analysis of the hierarchical systems used by each country for administrative regions and/or postal codes, and others. The FGC-IGC partner plans also to define a subsample of the IMS participants to have laboratory confirmation that will help the validation of the IMS results.

Task 5 (AIBV, FGC-IGC): Testing. The IMS in 'new' countries is tested by the local coordinator with assistance of Dutch / Portuguese IMS team in the 2010 season, preparing for the 2010 – 2011 flu season. The IMS platform need to tested to allow the assessment of software stability, database reliability and tune the advertisement campaign according to the various national habits and Internet penetration. This test run are usually made with a limited number of users and are done before the launch of massive data gathering campaigns.

Task 6 (AIBV): Implementation of the internet-based monitoring system in the five 'new' IMS countries starting in 2010. Subdivision:
In the 2010-2011 season, we will start implementing the IMS with local coordination in Sweden (partner SMI in WP6, task 6.1), UK (LSHTM), and France (to be selected subcontractor in 2009). Of course, this will be continued for the flu seasons in the subsequent three years of the project.;
From 2011 onwards, we introduce IMS in Germany (2011) and Spain (2012) with local coordination, through still to be selected subcontractors. Besides the effort required for the adaptation and implementation of the IMS in the new countries, this Task will strongly focus on communication and recruitment, as the previous experiences in the 'old' IMS countries showed that this is the key to the successful functioning of the surveillance system. Each local IMS will become a rich source of general information about influenza – scientific, medical, historical as well as social – constantly updated according to the latest information available. All the deployed content will have a local target as well as a european characterization as users become aware of the more general aim of the project they are participating at. To foster participation, educational activities for children and adolescents will be implemented and debates with the general public will be conducted. The necessary outreach will be again designed and implemented taking into account the different targets in the different countries.

Task 7 (CREATE-NET): Development and implementation of innovative non-intrusive data gathering solutions, based on the use of mobile phones. Mobile phones can be used to run simplified versions of influenzanet, providing access to the project to a much larger fraction of the population, also to the people who do not have access to the web. The information will be aggregated and transmitted through the fixed infrastructure (i.e. GPRS or GSM network) to the data center where it will be processed and included in the database. Research will be performed in order to design a simplified version of the survey still keeping the

crucial information needed for surveillance. Human-computer interaction effort will be made necessary to develop an interface that is easy to access to all sorts of users, also the non-experts, without resulting intrusive. Communication of the newly developed system running on mobile phones will be crucial to advertise the new method and recruit a larger part of the population. Analysis of the datasets containing information on the users participating to the surveillance system through the Internet or though the mobile phones will uncover analogies and differences in the type of users, biases in the stratification of the population more interested in one or the other method, comparison of the surveillance data obtained through the two methods for validation and understanding. Different degrees of success of the newly implemented technology in the various countries will provide material for further development of better surveys and recruitment methods in each local framework.

Task 8 (CREATE-NET, ISI): Development of software for contacts pattern detection. The widespread diffusion of mobile phones with Bluetooth technology can be used to gather data about the contact patterns among people in modern society. An application will be developed to detect contacts with other Bluetooth devices (meant to indicate proximity with another human being) and to save this information in the permanent storage of mobile devices. The properly anomymized data that are collected will be delivered to a central database and processed to extract meaningful indicators. These can be used in WP4 to enhance models with realistic patterns of “random” encounters among people and provide information on the “social attitude” of users, thus contributing to further elaborate the modelling of realistic people’s behaviour.

Task 9 (FGC-IGC): IMS for respiratory allergies and diarrhoeal infectious. Real-time measurements of airborn allergens, such as pollens, are typically obtained at low resolution while more refined distributions can be obtained through modelling of particle dispersal. The development of an internet-monitoring system based on questionnaires regarding specific allergy symptoms will enable not only the inference of pollen distribution for model validation but, more importantly, its impact on disease. The system will be designed and implemented in Portugal based on previous experience with Gripenet. The commonality of diarrhoeal diseases is also highly suggestive of the suitability of a similar approach in this context. Extensions will be designed and discussed within the consortium.

Task 10 (LSHTM): Extension of IMS to gather contact pattern data and household data
We propose to extend the functionality of the Influenzanet system to collect the following additional data:
• Contact pattern data from a panel of volunteers. Including records of who was contacted (spoken to or touched) in the previous day, the frequency of such contacts, and basic details such as age group and location of contact. This information would be used to parameterise mathematical models of the transmission of close-contact infectious diseases. Furthermore, the information will be used to establish the risk of infection (or self-reported disease) with the behaviour of the individual.
• Recruitment of a panel of households, and reporting of illness in household members to establish transmission coefficients with and between households, secondary attack rates, and generation time estimate.

Deliverables

5.1 Design of the ‘golden standard’, design and implementation of an internet database with English language documents (month 12).
5.2 Extension of IMS for collating contact pattern information and household influenza transmission data (month 12).
5.3 Tests run in 2009 (month 20).
5.4 Extension of IMS by mobile phones’ data gathering (month 20)
5.5 Tests run in 2010 (month 32).
5.6 Design and implementation of software for contacts patterns detections (month 32)
5.7 Gradual implementation of IMS and its internet database from 2010 onwards: well operating systems in five ‘new’ countries and in the four ‘old’ countries in 2013 (month 48).

WP 6 – Reporting systems comparative analysis and validation

Work package number	6	Start date or starting event:		Month 1		
Work package title	Reporting systems comparative analysis and validation					
Activity type[16]	RTD					
Participant number	7	1	2	5		
Participant short name	SMI	ISI	FGC-IGC	AIBV		
Person-months per beneficiary	128	12	2	6		

Objective

This WP is meant to provide a comparative analysis of *three* systems in Sweden: (1) the existing GP sentinel system of influenza surveillance with the (2) new internet monitoring system (IMS) and (3) a population-based approach, currently being evaluated on a large-scale pilot study basis.

In Sweden, these three influenza surveillance systems are the key elements of a comparative analysis by our consortium partner SMI with regard to IMS. They will carefully examine the three systems and evaluate the end results.

A fundamental prerequisite for surveillance-driven modelling is that there are surveillance data on incidence rates in important substrata of the population, defined in terms not only of geography and simple demographic features like age and sex but also of socio-economic structure related conditions like education, occupation (related to contact structure), household size, housing, commuting habits, smoking/non-smoking, vaccinated/unvaccinated, presence of chronic diseases/no such presence, etc. But even more important is that these rates are valid. The IMS is based on "opportunistic reporting", and acknowledging the promising data that have emerged upon the so far limited efforts to investigate the validity, it has not been shown beyond doubt that important selection forces aren't in operation. The only way to get truly valid rates is to ensure that they are obtained in a representative sample of the target population. Sweden, with its efficient population administration, unique national registration numbers assigned to all residents immediately after birth or immigration, and a long-since established complete and rapidly/continuously updated computerized population register, offers exceptional opportunities to obtain representative samples of the population. This, in turn, opens almost unique opportunities to investigate the validity of the IMS surveillance scheme. By performing a truly population-based disease surveillance (in a random and controlled sample of the population) in parallel with the IMS surveillance program, we will be able to shed better light on the issue of systematic errors in the rates. This will based on an accurate statistical comparison of different methods by following a specifically devised sampling and statistical protocol. Ideally, the validation effort will result in correction factors that will allow us to re-calibrate the IMS data. Then, population-based schemes might have to be considered in the other European countries as well.

Description of work

The internet-based monitoring system (IMS), as elaborated in the previous WP, is meant to cope with these limitations. However, as possible biases linked to the self-selection into IMS remains a potential concern, despite reassuring – but limited – data to the contrary, the Swedish partner will (1) set up the IMS system in Sweden, and (2) supplement the scheme with a population-based approach (PBA), based on experiences from large-scale pilot studies involving approximately 3,500 randomly selected individuals in Stockholm.

This will add to the validation of the IMS and may permit future calibration of the IMS data. In a PBA limited to Stockholm, a representative reporting cohort will be established through random sampling of

[16] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

approximately 5,000 individuals (all ages) from the complete and continuously updated population register. The selected individuals (or for children, their parents) will be approached via regular mail and asked to self-report infectious disease symptoms on an event-driven basis, either via internet or by an automatic interactive voice response system using regular telephones. At entry into the cohort, the selected individuals will complete a web or paper questionnaire with questions that cover information about sociodemographic data, previous infectious disease history, presence of chronic diseases, information about household and housing, lifestyle-related factors, work-related factors, contact pattern, physical characteristics of the workplace, commuting habits, etc. As part of the participant-initiated notifications, a tree-structured set of symptom questions are answered. The participants will remain in the cohort for one year and will be kept alerted to their task through irregular reminders, as developed and tested in previous large-scale pilot studies. In order to get more information about the course of the disease, to yield information about secondary cases in the household, if any, and also to address the role of transient variations in exposure precipitating clinical disease development, we will further automatically send out a web-based or paper questionnaire to the affected individual upon the receipt of a report. The questionnaire is to be answered on the 3rd day after disease onset. Therein, some exposures during days 2-5 prior to disease onset will be revisited in greater detail: presence/absence of infections in the household, at school/workplace, activities engaged in, the number and character of direct contacts, direct contacts with seemingly infected individuals at school/work, handshakes, modality of commuting, and some physical characteristics of the school/worksite.

An overall, comparative analysis of the three systems in Sweden should provide the key input to an evaluation of (ICT aided) influenza monitoring systems such as IMS and PBA. All tasks are implemented by SIDC unless otherwise indicated.

Task 1 (SMI): To obtain ethical approval for the IMS and PBA surveillance. Implement the IMS in Sweden.

Task 2 (SMI): To reach a business agreement with the subcontractor that provides the telecommunication and computer infrastructure for the PBA. To set up the Interactive Voice Response telephone system, the secure website, the response database, and the reporting system.

Task 3 (SMI): To draw a random sample of the Stockholm population and approach the selected individuals with invitations (and reminders as indicated) via regular mail (recruitment of the PBA cohort).

Task 4 (SMI): To administer the PBA system during 12 months, including activities aimed to keep up the participants' attention to the study.

Task 5 (SMI): To send out and collect postal or Internet-based validation questionnaires about the occurrence of infectious disease symptoms in the previous week.

Task 6 (SMI, AIBV, ISI, FGC-IGC): To clean the datasets and to compare data obtained through IMS, PBA and reports from the sentinel GPs and laboratories. Statistical analysis and report writing. Data provided to WP3 and WP4 for visualization and simulations.

Deliverables

6.1 A fully functioning technical infrastructure for the PBA surveillance (month 12)
6.2 A fully functioning and tested IMS in operation in Sweden (month 24)
6.3 The PBA cohort established (month 24)
6.4 The validation study of the PBA surveillance concluded, and the digitalized dataset delivered (month 36)
6.5 Academic papers on the validity of the PBS and on the concordance between results from IMS, PBA, sentinel system and laboratories (month 48).

WP 7 – Management

Work package number	7	**Start date or starting event:**		Month 1			
Work package title	**Management**						
Activity type[17]	MGT						
Participant number	**1**	2	3	4	5	7	12
Participant short name	**ISI**	FGC-IGC	TAU	MPG	AIBV	SMI	FFCUL
Person-months per beneficiary	44	4	4	4	4	4	4

Objectives

To coordinate the administrative and scientific work of the project.
To ensure that the management plan is carried out.
To monitor the project and correct deviations from project goals.
To coordinate the interaction with the Commission.
To coordinate the meetings with the steering committee.
To continually monitor and assess the project's progress in the terms of the stated work package objectives.
To coordinate the evaluation reports to the Commission as required.
To ensure the delivery of the annual progress report containing the activities (including those with no specific deliverable in that reporting term) and the assessment and lesson learnt for CS science.

Description of work

Task 7.1: provide co-ordination of administrative and scientific work, including the consortium meeting and the commission evaluation reports. It will also provide the interface with the Commission and to the media. Staff in this work package is responsible for the evaluation of the project in a continuous fashion through the assessment of the actually reached results versus the project objectives and, more in details, the objectives of individual work packages.A framework for the communication within the consortium participants as well as the associated partners will be set up from the very beginning. The internal user area of the project web site will be used for the exchange of information between the partners keeping them updated about the work in progress and providing assistance on development of special working groups. A yearly Management Report detailing all management activities (not directly content-related) and covering all deliverables of management type specific to the project will be provided.

Task 7.2: The management will also prepare yearly progress report aimed at accounting for RTD activities with no specific deliverables in the reporting periods and a summary of the lesson learned in CS from the project as well as the impact and advances with respect to the prediction and predictability of complex systems. The report will also focus on the project impact on the cycle technology-society-technology.

A detailed description of the EPIWORK management structure and procedure is given in Section 2.1.

[17] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

Deliverables
7.1-7.4 Yearly management reports (month 12, 24, 36, 48). 7.1-7.8 Yearly activity report with assessment of lesson learned (month 12, 24, 36, 48).

WP 8 – Dissemination, collaboration and exploitation

Work package number	8	**Start date or starting event:**		Month 1				
Work package title	**Dissemination, collaboration and exploitation**							
Activity type[18]	RTD/OTHER							
Participant number	**1**	2	3	4	5	7	8	11
Participant short name	**ISI**	FGC-IGC	TAU	MPG	AIBV	SMI	KUleuven	CREATE-NET
Person-months per beneficiary	24	24	2	2	22	18	3	2

Objectives

The goal of this work package is to make sure that the results achieved by the project are widely disseminated and can constitute the basis of other research across the scientific and engineering communities. The WP will also supervise the joint collaborative efforts with similar FET projects and the proactive FET initiatives and projects on science of complex systems for socially intelligent ICT. This WP will also ensure the delivery of the annual Dissemination, collaboration and exploitation report.

Description of work

Task 8.1 Project Presentation. This task will involve the preparation and circulation of a brief project presentation accessible to the non-specialist, avoiding technical language and high level mathematics as much as possible. It will be published via the World Wide Web and supplied in printed form to the Commission if requested. It will be intended for policy makers and disease management professionals, and researchers in the field of infectious diseases. Analogously, a final non-technical report summarizing the results achieved by the project will be provided at the end of the consortium activity.

Task 8.2 Dissemination strategies and social impact The Consortium will address the issue of using and disseminating knowledge through the lifetime of the project. This will include coordinating the dissemination of the project's achievements for the consortium as a whole, or for individual participants or groups of participants by regular scientific papers, editorial material and regular press releases on major results achieved. As much as possible we will exploit communication media to reach the largest possible audience. The project will put great emphasis on publication in high impact scientific and engineering communication channels. It also envisions communicating results at top international conferences. Progress will be regularly communicated to a wide audience on the Web page of the project, with announcements of public releases, of publications of academic papers, of presentations at international workshops. This implies the establishment of communication tools such as the web site, which is going to be for the general public health interested reader and the internal work of the consortium. Public health interested entities will have the opportunity not only to follow the development and the current results of the ongoing work of the

[18] Please indicate one activity per work package:
RTD = Research and technological development; DEM = Demonstration; MGT = Management of the consortium; OTHER = Other specific activities, if applicable in this call, including any activities to prepare for the dissemination and/or exploitation of project results, and coordination activities.

consortium but also to engage and interact with the different participants of the network with questions, suggestions, and promoting discussions. In addition, regular progress reports will be produced by the various working groups. These will be discussed and reviewed with the steering committee and will be circulated widely. These reports will be accompanied by short descriptions such as an executive summary, specifically made for policy makers where the major points will be emphasised and their implications for policy making at all levels – regional, national and Europe-wide – will be explained. Policy makers will be encouraged to assess the value of the newly developed systems for epidemic monitoring, simulation, and forecasts in managing the risks of infectious diseases. The project will take a particular care in exploiting the potentiality of the IMS recruiting to use the web tool as a podium for advertisement and dissemination of the project results. At the same time the web tool will be exploited to amplify the public perception on the issue of communicable diseases and a s a new media for information and risk awareness campaigns. The project will also jump start form the very beginning the contact and involvement of policy makers with the aim of defining a cornerstone of a consistent policymaking process informed by the integration of complex systems science in a socially-intelligent approach to disease forecast. A consequent impact will be improved preparedness, cooperation on required resources, logistic support and other associated processes in the context of infectious disease prevention and mitigation. These activities will amplify the impact of the of the project in the development of an European wide capacity in policy making and interaction with the society, using computational thinking and complex systems science. All the results obtained in these areas will be summarized in the yearly dissemination, collaboration and exploitation report.

Task 8.3 Training activities The training activities will include: (i) training activities for the researchers hired within the project, (ii) coordination of the staff exchange among the partners of the consortium, iii) the organisation of a midterm and a final year workshop aimed at involving the scientific community in the research of the consortium. It is worth remarking the value of a truly interdisciplinary training of the hired personnel. In addition, training activities are foreseen in the context of conferences or other kinds of gatherings, for example in the form of tutorials, emergency planning exercises, contributions to summer schools, etc. Especially relevant will be the presentation of the platforms developed in the project through schools which will introduce young scientists from a variety of different disciplines to the state-of-the-art epidemic research tools and methods. The Epidemic Modelling Platform will also be used in the teaching of classes related to epidemic modelling.

Task 8.4 Joint collaborations with related proactive FET projects and initiatives. The effort in this area will be devoted to exploration of collaboration avenues with other projects and the embedding of the Epiwork activities in the proactive FET projects, coordination action and eventual initiatives on science of complex systems for socially intelligent ICT such as a common web portal for projects and FET conferences. This will include the active participation and coordination of joint activities such as cluster meetings and/or training programs. The exchange of students and researchers in order to create strong ties among related projects and the eventual work toward joint publication will be fostered. Finally, the project will participate to the development of a common roadmap for future research in the domain related to the project work.

Deliverables

8.1 - Project presentation report (month 4).
8.2 - Project web site (month 8)
8.3 - Mid-term workshop (month 24).
8.4 - Final year workshop (month 44).
8.5 - Final non-technical report on the project (month 48)
8.6-8.7-8.8-8.9 Dissemination, collaboration and exploitation report (month 12,24,36 and 48).
8.10 – Preparation of collected papers book (edited by the project Chairs) highlighting the major advances and specific contributions of the project to the field (month 48).

B.1.3.6 Efforts for the full duration of the project

Part no.	Partic. short name	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	Total PMs
1	**ISI**		(24)	24 (36)	36 (36)	24 (12)	(12)	36 (8)	12 (12)	132 (140)
2	**FGC-IGC**	40 (12)	48 (8)	(4)	8 (4)	80 (8)	(2)	(4)	16 (8)	192 (50)
3	**TAU**	70 (26)	30 (16)	8	36 (16)			(4)	(2)	144 (64)
4	**MPG**		60 (42)	18 (24)	18 (24)			(4)	(2)	96 (96)
5	**AIBV**			2 (2)		50 (10)	4 (2)	4	10 (12)	70 (26)
6	**LSHTM**	25.5				25.5				51
7	**SMI**						62 (66)	(4)	10 (8)	72 (78)
8	**KULeuven**					24			(3)	24 (3)
9	**BIU**	25 (5)	20 (5)	10 (1)	25 (5)					80 (16)
10	**FBK**		13.5	6	25					44.5
11	**CREATE-NET**					36			2	38
12	**FFCUL**	24 (18)		60 (22)	12 (7)			(4)		96 (51)
total		184.5 (61)	171.5 (95)	128 (89)	160 (92)	239.5 (30)	66 (82)	40 (28)	50 (47)	1039.5 (524)

Each cell in the table contains 2 numbers: the first number corresponds to the number of person months (PMs) derived from the EC requested contribution, whereas the second – in brackets – corresponds to the number of PMs not from EC contribution.

Project Effort Form 2 - indicative efforts per activity type per beneficiary[19]

RTD/Innovation activities	ISI	FGC-IGC	TAU	MPG	AIBV	LSHTM	SMI	KULeuven	BIU	FBK	CREATE-NET	FFCUL	
WP 1 – Population models and contact networks		40 (12)	70 (26)			25.5			25 (5)			24 (18)	184.5 (61)
WP 2 – Spatially structured models and human mobility	(24)	48 (8)	30 (16)	60 (42)					20 (5)	13.5			171.5 (95)
WP 3 – Information platform	24 (36)	(4)	8	18 (24)	2 (2)				10 (1)	6		60 (22)	128 (89)
WP 4 – Epidemic Modelling Platform	36 (36)	8 (4)	36 (16)	18 (24)					25 (5)	25		12 (7)	160 (92)
WP 5 – ICT monitoring and reporting system	24 (12)	80 (8)			50 (10)	25.5		24			36		239.5 (30)
WP 6 – Reporting systems comparative analysis and validation	(12)	(2)			4 (2)		62 (66)						66 (82)
Total 'research'	84 (120)	176 (38)	144 (58)	96 (90)	56 (14)	51	62 (66)	24	80 (16)	44.5	36	96 (47)	949.5 (449)

19 Please indicate in the table the number of person months over the whole duration for the planned work , for each work package, for each activity type by each beneficiary

Consortium activities	ISI	FGC-IGC	TAU	MPG	AIBV	LSHTM	SMI	KULeuven	BIU	FBK	CREATE-NET	FFCUL	
WP 7 - Management	36 (8)	(4)	(4)	(4)	4		(4)					(4)	40 (28)
WP 8 – Dissemination, collaboration and exploitation	12 (12)	16 (8)	(2)	(2)	10 (12)		10 (8)	(3)			2		50 (47)
TOTAL BENEFICIARIES	132 (140)	192 (50)	144 (64)	96 (96)	70 (26)	51	72 (78)	24 (3)	80 (16)	44.5	38	96 (51)	1039.5 (524)

B.1.3.7 - List of milestones and planning of reviews

Milestones

Milestones are control points where decisions are needed with regard to the next stage of the project. For example, a milestone may occur when a major result has been achieved, if its successful attainment is a required for the next phase of work. Another example would be a point when the consortium must decide which of several technologies to adopt for further development.

Milestone number	**Milestone name**	**Work package(s) involved**	**Lead beneficiary**	**Delivery date from Annex I**	***Comments***
1	Models of disease transmission under seasonality and other	1	TAU	Month 36	Validated models published in academic papers.

	external drivers				
2	Theoretical foundation and mathematical description of network-network systems, i.e. spatially embedded contact networks and empirical validation by case study of respiratory diseases in the UK.	2	MPG	Month 24	Validated models published in academic papers.
3	Theoretical foundation and mathematical description of multiscale transportation networks	2	MPG	Month 36	Validated models published in academic papers
4	Epidemic Marketplace Platform with initial an initial set of epidemiological databases integrated available to project participants .	3	FFCUL	Month 12	Prototype validated by the Consortium
5	Public release of Epidemic Marketplace Platform.	3	FFCUL	Month 20	Public release
6	Prototype modelling suite of the Epidemic Modelling Platform programmed including contact patterns and population movement as emerging from WP1 and WP2, with documentation	4	ISI	Month 20	Prototype validated by the Consortium
7	Public release of Epidemic Modelling Platform including contact patterns and population movement with documentation integrated with sophisticated visualization techniques.	4	ISI	Month 32	Public release
8	Design and implementation of an internet database with English language documents	5	AIBV	Month 12	Public release
9	Implementation of a database infrastructure for ‘new’ IMS countries.	5	AIBV	Month 24	Public release
10	Final implementation of IMS and its internet database in 2011/2012: well operating systems in five ‘new’ IMS countries and in the four ‘old’ IMS countries.	5	AIBV	Month 40	Public release

11	A fully functioning technical infrastructure for the PBA surveillance in Sweden.	6	SMI	Month 12	Public release
12	The IMS and PBA surveillance concluded in Sweden, and the response dataset delivered to the investigators.	6	SMI	Month 36	Validated analysis published in academic papers

Tentative schedule of project reviews			
Review no.	**Tentative timing, i.e. after month X = end of a reporting period**	***planned venue of review***	***Comments , if any***
1	After project month: 12	**TBD**	
2	After project month: 24	**TBD**	
3	After project month: 36	**TBD**	
4	After project month: 48	**TBD**	

Note: This is a new table which was not included in the proposal.

B2. Implementation

B 2.1 Management structure and procedures

The project management approach considered for Epiwork is based on well consolidated management plans and techniques, which have been used successfully in previous international projects. The primary goal of the chosen management structure is to be capable of responding to the needs of an Integrated Project without imposing intrusive or costly time and resources overheads. Flexibility is one of essential aspect considered in defining this structure.

The management of the project can be divided into three different categories.

Project Management: This category encompasses the day by day management of the project, the coordination of the management efforts and the communication within the consortium.

Financial Management: This category encompasses for the control of overall project expenditure, as well as for cost report collection, check and payment.

Scientific Management: This category encompasses the co-ordination of operative efforts within a scientific and technical scope, including the responsibility for the scientific and technical decisions taken in the project and the control and corrections of these decisions.

The management structure of the consortium includes the **Project Coordinator**, the **Steering Committee,** and **the project board.** An important role is attributed to the **WP-leaders** who are responsible for the WP coordination. The project will be managed by the ISI Foundation, **the Coordinator**, which has a long experience and well established procedures for managing European projects. The coordinator appoints as **project coordinator** Alessandro Vespignani. A consortium agreement will provide rules and terms of reference for any issue of legal nature concerning the co-operation among the parties as well as the intellectual property rights of individual partners and the consortium as a whole.

The **project coordinator** has the overall responsibility for the project. He will be the main interface between the project and the European Commission and will communicate all information in connection with the Project to the Commission. Among other tasks the project coordinator will have the following primary duties:

- Administration and co-ordination of the project resources.
- Coordinate and oversee the work in all work packages.
- Organization of regular meetings of the steering committee for detailed discussion of the results and further planning of the work.
- Set up of a framework for communication amongst the consortium participants as well as with associated partners. This includes the establishment of communication tools such as the web site, whose internal user area will be used for the exchange of information between the partners, keeping them updated about the work in progress and providing assistance on development of special working groups. The site will be registered in the .eu domain.
- Prepare the Yearly Management Report that will detail all management activities (not directly content-related) and cover all deliverables of management and dissemination type specific to the project. These include a report on results (data, software) available to all other projects, a quantitative assessment: How many articles were published? How many in the specialised press, how many in the non-specialised press? What strategy and what actions were taken to attract the press? What actions were taken to exploit the project results?

The **project coordinator** will provide unique e-mail address (epiwork@isi.it) that will be used for all official communications regarding the project. The project coordinator will take advantage of the ISI internal management structure to delegate specific tasks to a **financial manager** and a **project manager** (see Diagram 3).These delegated tasks includes but are not limited to:

- Arrangement of meetings and minutes-related activities.
- Issuing of periodical reports.
- Billing of efforts and budget.
- Financial management activities
- Acting as interface between the consortium and the financial department of the co-coordinating partner in order to ensure that all payments are properly performed, that the appropriate amounts were received by partners (except, if any, problems between the affected partner and its own bank).etc.

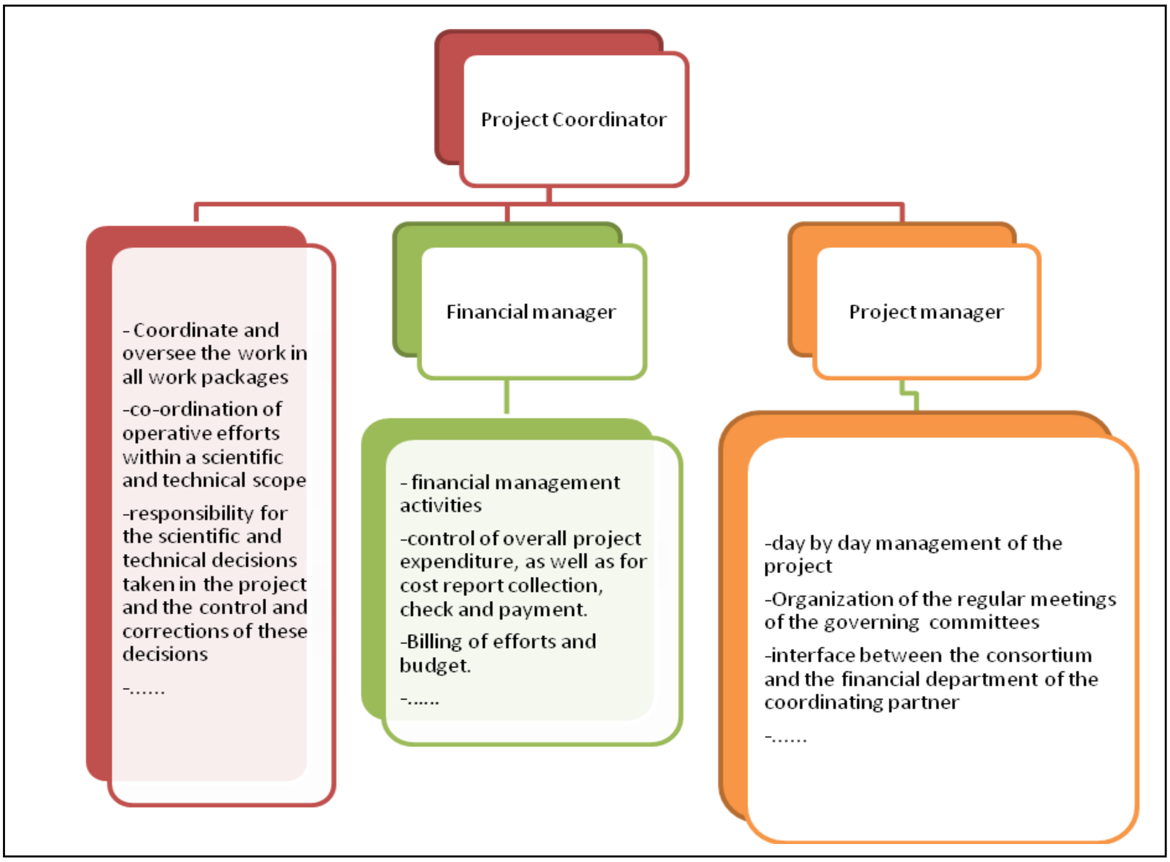

Diagram 3: Management structure of the coordinator ISI foundation.

The **WP-Leaders** are responsible for the respective WPs by ensuring the scientific and/or technical overview of the progress in each Work Package.

Among their typical tasks;

- Lead the scientific and technical issues in a given work package.
- Definition and follow-up of Work Package progress and objectives.
- Transmission of any document or information to the other Work Package Leaders concerned with the scientific work of the WP.
- Transmission of any document or information to the contractors concerned or to the Work Area Leader
- Responsibility for the day-to-day technical management of the work package.

The **steering committee** (SC) assists the Coordinator and is the governing scientific and technical body of the project. The full SC is formed by the **chairs** and the **WP-leaders**. It is chaired by the **project coordinator appointed by the coordinator** and the **co-chair**. The presence of two chairs is motivated by the multidisciplinary vision needed in EPIWORK in order to have a quick assessment and management of the various aspects of the project. The Chair (project coordinator) is a senior computational modellers, physicists and informaticians and the leader of the ISI team and

the co-chair is a senior theoretical epidemiologist and the leader of the FGC-IGC team in this project and is currently the leader of a Marie Curie Excellence Team.

Among the SC tasks

- Project Plan;
- Deciding on technical roadmaps for the project;
- Monitoring international developments on data/modelling interfaces and organising one scientific workshop with external experts on Internet measurements and modelling;
- Ensuring the dissemination of results of the project and information deemed valuable for the consortium;
- Overseeing and reviewing the work progress and deciding on overall technical matters;
- Consolidating the reports received from the work package coordinators and preparing the reports and deliverables to be submitted to the European Commission.
- Creation/Termination of tasks.
- Decisions to abandon specific deliverables.

The **chairs** and the **WP leaders** will be in close contact at all stages of the project and will take care of monitoring constantly the detailed progress of the WPs and will promptly initiate corrective actions if needed. Decisions will be taken during meetings (face-to-face or via conference call). The SC will meet when needed once every year (ordinary) and on any project board member's demand (extraordinary) with a pre-notice of minimum 15 natural days (ordinary), and 5 working days (extraordinary). Meetings' Agendas are proposed by the Chairs 5 working days in advance to the SC designated meeting date. Decision will be taken by voting with the "One member, one vote" scheme on the basis of absolute majority (Half+1).). In the case of a tie the project coordinator will have the casting vote.

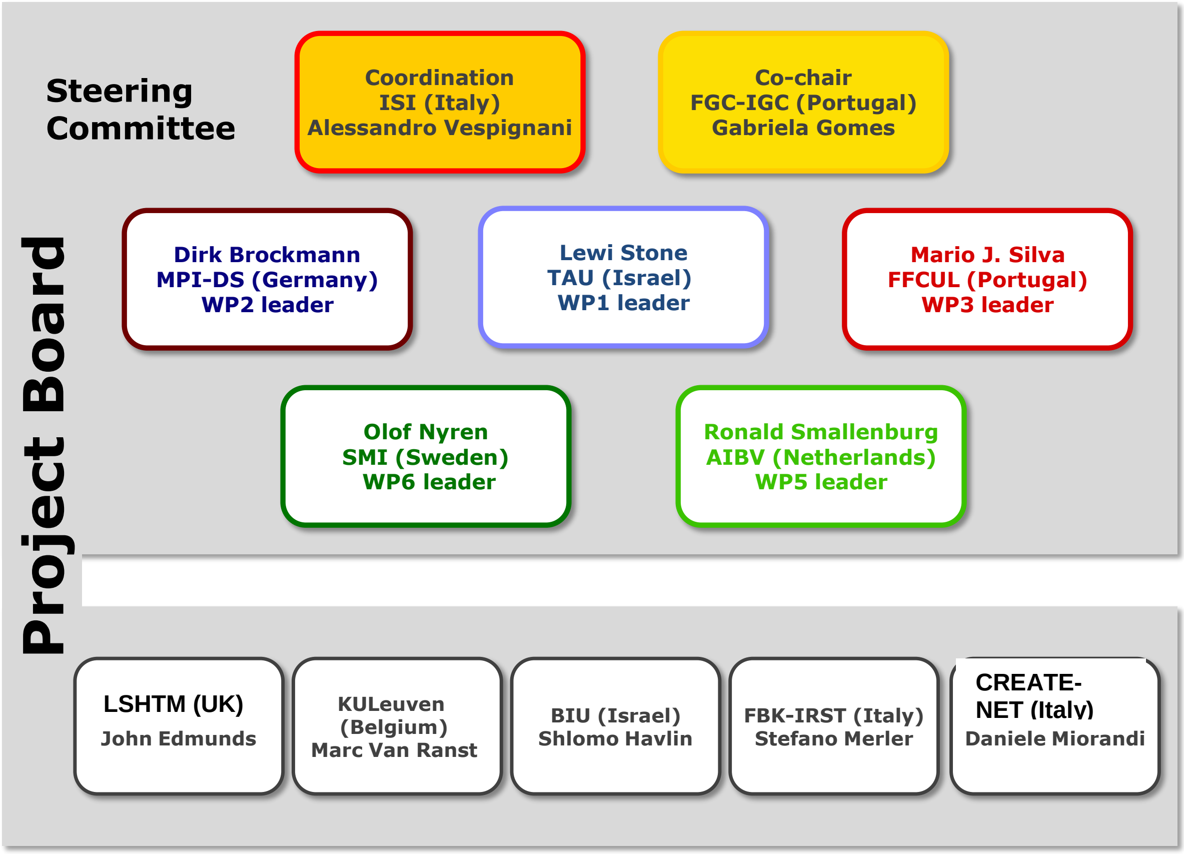

Diagram 4: Illustration of the project management structure

The diagram shows the management structure of the consortium, including the Project Coordinator, the Steering Committee and the Project Board. WP leaders and team leaders are shown.

The **project board** is formed by the **SC**, and the **lead scientists** of each team participating in the consortium. The financial manager and project manager will be non-voting member of the scientific board. It is the governing body for the overall direction and major decisions of the project and the communication, control and corrections of these decisions.

It will be responsible to take major decisions, such as:

- Budget transfers
- Termination of the Contract
- Actions against defaulting partners
- Selecting new contractors to enter Contract and Consortium Agreement.
- Important Changes (Budget or Work Shares affected >10%) in the Project and/or Amendments to the Contract
- Decisions related to dissemination, training and exploitation activities

The project board will meet each year and whenever it is requested by the Steering committee (extraordinary) with a pre-notice of minimum 15 natural days (ordinary), or 5 working days (extraordinary). The agenda is proposed by the Steering Committee + suggestions from partners and will be available at least 5 working days before the meeting. Voting must be identified as such in the

agenda. If not foreseen, agreement about voting is also possible during the meeting itself, if so agreed (unanimously). Decision will be taken by voting with the “One member, one vote” scheme on the basis of absolute majority (Half+1). In the case of a tie the project coordinator will have the casting vote .

The Annual ordinary meeting will be the natural yearly check and self-assessment moment for the Consortium. It will serve to enhance the exchange of scientific information and to foster discussion and to critically review the scientific and organisational matters of the Consortium. The annual meeting will be also used as an occasion to gather all the participants to the project in a parallel workshop with presentations of the achievements of the individual Work Packages. All participants, including associates are strongly encouraged to participate in the workshop.

Measurement of project progress

As described above, each Work package Leader is responsible for the compliance of his/her own Work package. Further, the consortium will use typical measures such as milestones within the project plan. Each member of the consortium will be responsible for informing the project coordinator and the SC chairs about any contingencies that might have negative impacts on the success of the project. Standard and commonly available project management software tools will assist project management. The measurement of the project progress will be done internally with the following yardsticks:

- Timely completion of the work packages and tasks.
- Use of the resources according to the work plan.
- Satisfaction of the users expectations with the progress of the project.
- Reaction from industry and interest from other European organisations involved in Assisted Living on project results (after dissemination activities).

It will be the responsibility of the coordinator to keep track of these measurements during the full project and take the necessary actions in case of unsuitable progress.

The project will also rely on an **external advisory board**. The Advisory Board will consist of technical and research experts of high international expertise and relevance appointed by the project. It will have representatives from the ECDC and the JRC, the full list of appointed advisors will be formalized in a collegial way during the kick-off meeting of the project. The external advisory board will be in charge of advising on the roadmaps for the scientific and technical activities. It will report to the SC and will also advise on policy-related, scientific or technical subjects as identified and requested by the SC. The participation of the Advisory Board can be in different ways: Meeting; Workshops; Document reviews. Different Advisory Board members can be invited to participate depending on the subject to be dealt in the activity.

Conflict resolution and risk management

During preparation of the proposal, all the consortium partners have elaborated a common understanding of the goals to be achieved within Epiwork. The procedure for constantly updating the common understanding will be conducted during the whole project and will ensure Epiwork has constancy of purpose. The Project Board will have responsibility to solve any conflict that arises during the project execution and in the case that agreement cannot be reached, the Project Coordinator will define the measures to be adopted.

B2.2 Beneficiaries

1. ISI - Institute for Scientific Interchange Foundation, Italy

Team Leader: Alessandro Vespignani, Institute for Scientific Interchange and Indiana University.
Web page: http://www.isi.it; http://cxnets.googlepages.com/

The ISI Foundation (www.isi.it) is a private research institution located in Turin, Italy. It is founded and supported by the Regional Government, the Province of Turin, the City of Turin, and by the two major Bank Institutions in Piedmont – San Paolo and CRT Foundation. Its mission focuses on promoting scientific interchange and cooperation at the highest degree of quality both in terms of creativity and originality of research. It aims to represent a pole of high level interdisciplinary training in the fields of Mathematics, Physics, Computer Science, and Life Sciences. The ISI foundation has an extensive experience in the participation and management of European projects and at the moment is the coordinating centre of two coordination actions and participates to several STREPs and IPs consortiums within the EU 6th Framework Program. The ISI Foundation consists of four main research Divisions and nine laboratory/Units lead by international level scientists, while the SAB (Scientific Advisory Board) has the duty of identifying the research lines of the Institute.

The ISI research unit participating to this project, the complex networks Lagrange Laboratory (CNLL), gather an extensive range of scientific expertise in both areas of computational modelling of infectious diseases and in the development of cyberinfrastructure and data integration tools. The staff in the CNLL has applied these skills in the large scale simulation of emerging disease at the world-wide level, the study of transportation and mobility infrastructures on epidemic spreading patterns, census database integration, the development of data visualization techniques. The research activity of the CNLL also focuses on the study of the emergence, characterization and impact of complexity in biological and ecological networks and social/behavioral networks. Finally, the ISI team has been active in testing and deploying the Influweb monitoring platform (www.influweb.it).This platform is integrated with the analogous projects in the Netherlands and Portugal which are at the core of the WP4. The international nature of the Institut*e* allows the team to maintain ongoing collaborations with the National Institute of Health (INSERM) and the University of Paris-Sud in France, with the Indiana University and Boston University in the US, and with the Universitat Politecnica de Catalunya in Spain.

Role in the proposal: The CNLL brings skills and competence in the area of data and models integration as well as in Informatics and computational tools. The team has experience in theoretical and computational modelling of epidemics. The group is also active in the integration of transportation and demographic data in large scale epidemic stochastic models and is an expert in GIS interfaces and visualization algorithms. CNLL staff members are expert in automated data mining and aggregation and computational tools that support professional knowledge management. In this project the ISI team will have an active role in the WP2, WP3, WP4 and WP5. In addition, ISI foundation will coordinate the project and lead the management effort.

ISI team: ISI host a sizeable computational epidemiology group. **A. Barrat** will work on the theory of complex networks in epidemic modelling. **V. Colizza** (recently awarded a ERC grant on computational epidemiology) will lead the effort on the computational platform and in the large scale realistic modelling at ISI. **F. Gargiulo** and **J.J. Ramasco** will work on data gathering and integration on large scale models. **D. Paolotti** is the project manager working on the IMI deployment in Italy. **Alessandro Vespignani** is also professor at the School of Informatics of Indiana University, working on projects related to collaborative infrastructures for epidemic research and the study of social systems in Information technology networks. He is half time resident scientists at ISI and will ensure the lead of the whole project along with several international contacts outside Europe.

Most significant publications:

Colizza V, Barrat A, Barthelemy M, Vespignani A, Predictability and epidemic pathways in global outbreaks of infectious diseases: the SARS case study, *BMC Medicine* 5, 34 (2007).

Colizza V, Barrat A, Barthelemy M, Valleron A-J, Vespignani A, Modeling the Worldwide Spread of Pandemic Influenza: Baseline Case and Containment Interventions, *PLoS Medicine* 4(1): e13 (2007).

Colizza V, Barrat A, Barthélemy M, Vespignani A, The modeling of global epidemics: stochastic dynamics and predictability, *Bull. Math. Biol*. 68, 1893-1921 (2006).

Colizza V, Barrat A, Barthélemy M, Vespignani A, The role of the airline transportation network in the prediction and predictability of global epidemics, *Proc. Natl. Acad. Sci. (USA)* 103, 2015-2020 (2006).

2. FGC-IGC - Fundação Calouste Gulbenkian - Instituto Gulbenkian de Ciência, Portugal

Team Leader: Gabriela Gomes. Leader of the Theoretical Epidemiology Group and Marie Curie Excellence Team Leader, Instituto Gulbenkian de Ciência, Oeiras, Portugal.

Web page: http://sites.igc.gulbenkian.pt/ggomes/

The *Fundação Calouste Gulbenkian* (FCG) is a private non-profit organization with four statutory goals: "charity, art, education and science". The Gulbenkian Science Institute (*Instituto Gulbenkian de Ciência,* IGC) (hereinafter referred to as "FCG-IGC") was founded and is supported by the *Fundação Calouste Gulbenkian* to carry on biomedical research and education. The FCG-IGC operates as a "host institution", offering excellent facilities and services to foreign and Portuguese research groups or individual scientists, in particular to young scientists who are expected to develop and manage their research projects and form their groups in complete autonomy

The Institute's scientific interests are focused (i) on the genetic basis of development and evolution of complex systems, privileging organism-centered approaches in experimental models that include plants, yeast, worms, flies, fish, chick and mice, and (ii) on the genetics of complex human diseases. Other FCG-IGC specificities are the theoretical studies sector, although with a small dimension/ impact, the quality of the central services and facilities offered, and a strong investment on international exchange in the form of graduate courses, workshops and symposia.

In 2005, the IGC established the Collaboratorium in Computational Biology, an open host organization designed to enable intense cooperation amongst researchers from national and international institutions: the center hub of a collaborative network of research institutions. Its chief aims are to provide suitable facilities for visiting scientists, and hosting informatics technology to enable continuing off-site collaboration and research in Mathematical and Computational Biology.

Moreover, over the last few years, the IGC has developed a dedicated science communication programme to promote public engagement in science through direct, two-way communication between scientists and the public. This programme targets a range of audiences, including schools (students and teachers), the media, decision-makers, community and patient groups and the general public. Within this programme, the IGC holds interactive meetings between scientists and different publics, workshops and hands-on activities, open days, develops information materials and education resources. Recent activities include the publication of a teenage novel written in close collaboration with scientists and the start of a philanthropy/fundraising programme aimed at establishing alternative funding opportunities for scientific research, at the same time as further involving Portuguese society in science and scientific culture.

Role in the proposal: The IGC hosts the Theoretical Epidemiology Group since 2002 and the internet-based monitoring system for influenza, Gripenet, since 2005. The participation of the IGC in this project includes a vast spectrum of competencies: theoretical and computational modelling of infectious diseases; integration of models with data; implementation of ICT monitoring and reporting systems; science communication; engagement with schools. The ultimate goal of the IGC team is to provide the European Research Area with a flexible infrastructure for epidemic forecast. The team is working with public health institutes throughout Europe to prepare the ground to extend the theoretical and technological framework develop here into an effective interface between data analysts/modellers and public health decision makers.

FGC-IGC team: Gabriela Gomes, Ana Godinho. **Dr. Gabriela Gomes** is currently the Leader of the Theoretical Epidemiology Group at the IGC and a Marie Curie Excellence Team Leader. She initiated Gripenet in Portugal in 2005 and has since assumed the role of Scientific Coordination of the programme. She has launched the Lisbon Epidemiology Consortium in 2007 of which she is the Scientific Coordinator. Her research interests are focused on theoretical approaches to biomedical research. Her research group has a high turnover rate and currently counts 20 members: 6 postdocs; 4 PhD students; 4 prospective PhD students; 3 administrative and technical staff; and 2 visiting scientists. The group has made innovative contributions to the theoretical foundations of infectious disease epidemiology, as well as applications to tuberculosis, influenza, pertussis and malaria, and collaborates with universities and research institutes in Europe, America, Africa and Asia. In 2007, Gabriela initiated a series of initiatives to include Epidemic Forecast in the Road Map for European Infrastructures. The current proposal is one component of this wider effort. **Dr. Ana Godinho** is currently Science Communication and Outreach Manager for the FCG-IGC. In this role she coordinates media and external affairs, and Public Engagement in Science/Outreach. Ana has several years of professional experience in communicating science with the public and with the media. Before joining the FCG-IGC, she held a position in science communication at the Institute for Stem Cell Research in Edinburgh. Before becoming a science communicator, Ana obtained her PhD in Developmental

Neurobiology from the University of London and went on to do post-doctoral research at King's College London. Ana has run Open Days, debates and consensus conference-like meetings for the public, organised activities and workshops for students and teachers, is the co-author of a hands-on activities book for children and has developed dialogue-based educational resources. Ana also runs communication workshops for scientists. She has presented her work at international science communication meetings, published in science communication journals and co-authored book chapters. She collaborates with European organisations and networks, namely ESConet (European Science Communication Network) and EuroStemCell (European Consortium for Stem Cell Research).

Most significant publications:

Águas R, White LJ, Snow RW, Gomes MGM (2008) Prospects for malaria eradication in sub-Saharan Africa. *PLoS ONE* 3(3): e1767.

van Noort SP, Lourenço J, Rebelo de Andrade H, Muehlen M, Gomes MGM (2007) Gripenet: an internet-based system to monitor influenza-like illness uniformly across Europe. *Eurosurveillance Monthly*, Volume 12, Issue 7-8.

Gomes MGM, Franco AO, Gomes MC, Medley GF (2004) The reinfection threshold promotes variability in tuberculosis epidemiology and vaccine efficacy. *Proc. R. Soc. Lond.* B **271**, 617-623.

Coutinho AG, Araújo SJ and Bettencourt-Dias M, (2004) Science communication in Portugal: an evaluation of the prospects for two-way, direct communication between scientists and the public; *Comunicação e Sociedade* **6**:113-134

Bettencourt-Dias M, Coutinho AG and Araújo SJ (2004) Strategies to Promote Science Communication: Organisation and Evaluation of *"Comunicar Ciência"*, a Workshop to Improve the Communication Between Portuguese Researchers, the Media and the Public; *Comunicação e Sociedade* **6**:89-112

3. TAU - Tel Aviv University

Team leader: Lewi Stone

Web page: http://www.tau.ac.il/lifesci/departments/zoology/members/stone/stone.html

Located in Israel's cultural, financial and industrial heartland, Tel Aviv University is the largest university in Israel. It is a major center of teaching and research, comprising nine faculties, 106 departments, and 90 research institutes. With close to 30,000 students, the University offers an extensive range of study programs in the arts and sciences, within its Faculties of Engineering, Exact Sciences, Life Sciences, Medicine, Humanities, Law, Social Sciences, Arts and Management.

For more than ten years **Prof. Stone** has directed a Biomathematics Unit located in the university's Faculty of Life Sciences. The unit has broad interest in the epidemiology, population dynamics, and the evolution of infectious diseases, and in developing mathematical modelling and statistical techniques for analysing disease data. Much of the unit's work has been concerned with recurrent infectious diseases (measles, mumps and chickenpox), effective vaccination schemes and more recently influenza models. Highlights of their work include the development of pulse vaccination schemes, and predictive epidemic forecasting tools.

The unit has strong links with the Israel Center of Disease control (ICDC) and the Center's Director, Professor Tami Shochat, is involved with common projects. The unit also has a working collaboration with Dr. Eli Stern, and Dr. Amit Huppert in the Gertner Center of Health Risk Analysis, in joint projects on influenza dynamics in Israel.

Role in proposal: the Tel Aviv University Biomathematics Unit will be responsible for leading Work Package 1: Theoretical Foundations: Population Models and Contact Networks. This will involve developing new "cutting edge" modelling tools that combine population contact and network structures. In addition here will be a focus on nonlinear dynamical approaches for studying seasonally forced systems that take into account pathogen evolution, and epidemic models with reinfection. Prof. Lewi Stone will lead the team. Dr. Haggai Katriel, a mathematician, will work as a dedicated Research Associate on the project and will be primarily involved with mathematical modelling epidemic dynamics, from simple models to metapopulations. Dr. Asher Uziel, a postdoctoral fellow, will be concerned specifically with influenza models. Mr. Oren Barnea and Mr. Uri Roll are students just beginning their PhD's and will be concerned with the analysis and the modelling of extensive influenza data-sets collected in Israel over the last ten years. Mr. Rami Yaari and Mr. Or Givan are MSc Dr. Katriel and Stone, with the mathematical modelling.

TAU Team: Prof. Lewi Stone, Dr. Haggai Katriel, Dr. Asher Uziel, Uri Roll and Oren Barnea (PhD students), Rami Yaari , Or. Girvan (MSc students)

Most significant publications:

Stone, L., Shulgin, B. and Agur, Z. Theoretical examination of the pulse vaccination policy in the SIR epidemic model. Mathematical and Computer Modelling 31:207-215, 2000.
Artzy-Randrup Y., Fleishman S.J., Ben-Tal N. and Stone L. Comments on "Network Motifs: Simple Building Blocks of Complex Networks" and "Superfamilies of Evolved and Designed Networks". Science 305 : 5687. 2004.
Olinky R. and Stone L. Unexpected epidemic thresholds in scale-free networks. Physical Review E 70, 30902(R). 2004.
Stone L., Olinky R. and Huppert A. Seasonal dynamics of recurrent epidemics. Nature 446: 533-536. 2007.
Bunimovich-Mendrazitsky S, Shochat E, Stone L. Mathematical model of BCG immunotherapy in superficial bladder cancer. Bull Math Biol. 69:1847-70.2007.
Olinky R, Stone L. and Huppert A. Seasonal dynamics and threshold governing recurrent epidemics. 2008. J. Math. Biology..

4. MPG - Max Planck Institute for Dynamics and Self-Organization, Germany

Team Leader: Dirk Brockmann, Department of Nonlinear Dynamics
Web page: www.ds.mpg.de; www.nld.ds.mpg.de

The Department of Nonlinear Dynamics (NLD) is the theory department of the Max-Planck-Institute for Dynamics and Self-Organization (MPIDS) and was founded in 1996. Research conducted in the Department is primarily concerned with the dynamics of complex systems such as transport in nanostructures and quantum chaos and applying methods from nonlinear dynamics, complex network theory, non-equilibrium statistical mechanics and high performance computing to the study of complex biological networks and computational neuroscience. In 2003 a team of NLD lead by Dirk Brockmann initiated a scientific focus on the dynamics of human infectious diseases and anomalous dispersal phenomena in spatially structured systems. Today a substantial effort is devoted to this subject within the department. The team now consists of nine members (staff scientists, independent research fellows, postdocs and students) and closely collaborates with the independent research group "Network dynamics" lead by Dr. Marc Timme at the Institute and with Dr. Fabian Theis, head to the Research Group "Computational Modeling in Biology" at the Institute for Bioinformatics and Systems Biology at the Helmholtz Center in Munich, who is affiliated with the MPIDS as a Bernstein Fellow. In the past few years the group has published several influential articles on quantitative models of the worldwide spread of emergent human infectious diseases and statistical laws that underlie human travel behavior, fundamental theoretical results on synchronization phenomena in coupled network systems and the development of powerful numerical bioinformatic techniques in systems biology. NLD collaborates intensively with epidemiologists at the Center of Infectious Disease Dynamics (CIDD), USA and the Department of Zoology, Oxford as well as various groups across different disciplines.
Role in the proposal: The researchers at NLD will provide their expertise for the theoretical foci of WP2. The team has substantial experience in interdisciplinary research on network dynamics, anomalous diffusion and the development of high performance computer simulations and the application of methods from theoretical physics, statistical physics to the quantitative modelling of spatial dynamics of diseases. Furthermore, the team will be responsible for the design and implementation of large scale databases of transportation networks, proxy networks of human mobility and the construction of interface platforms for the transfer and embedding of these databases into the computation platforms designed in WP3. Dirk Brockmann is also professor for Complexity in the Department of Engineering Sciences and Applied Mathematics, Northwestern University and is affiliated with the Northwestern Institute for Complex Systems where he does research on network theory, anomalous diffusion phenomena, spatial linguistics and social dynamics on the interface of theoretical physics social science and biology. In this proposal the NLD team will have an active role in and lead WP2.
MPIDS team: M. Timme, F. Theis, D. Brockmann, V. David, V. Belik, B. Schwenker, A. Morales-Gallardo, R. Brune, C. Thiemann, Jan Nagler
Most significant publications:

P. Ashwin and M. Timme, *Nature* **436** (7047), 36 (2005).
D. Brockmann, L. Hufnagel, and T. Geisel, *Nature* **439** (7075), 462 (2006).
V. Belik and D. Brockmann, *New Journal of Physics* **9**, 54 (2007).
D. Brockmann and T. Geisel, *Phys Rev Lett* **90** (17), 170601 (2003).
D. Brockmann and T. Geisel, *Phys Rev Lett* **91** (4), 48303 (2003).

L. Hufnagel, D. Brockmann, and T. Geisel, *P Natl Acad Sci USA* **101** (42), 15124 (2004).
D. Brockmann and L. Hufnagel, *Physical Review Letters* **98** (17), 178301 (2007).
S. Jahnke, R. M. Memmesheimer, and M. Timme, *Physical Review Letters* **1** (4) (2008).
R. M. Memmesheimer and M. Timme, *Physical Review Letters* **97** (18) (2006).
M. Timme, *Physical Review Letters* **98** (22) (2007).
A. Zumdieck, M. Timme, T. Geisel et al., *Physical Review Letters* **93** (24) (2004).

5. AIBV - Acquisto Inter BV, Amsterdam, The Netherlands

Team Leader: Ronald Smallenburg
Web pages: www.degrotegriepmeting.nl; www.degrotegriepmeting.be; www.acquisto-inter.com
Acquisto Inter BV is a consultancy and project management firm in science and science communication. Among others, we are the organizers of the annual Grote Griepmeting (GGM) or Great Influenza Survey in the Netherlands and Belgium since 2003. The GGM is an internet-based monitoring system (IMS), including a weekly survey of influenzalike illness (ILI) . It was an instant success with over 31.000 Dutch and Belgian volunteers (so called 'flu meters') filling in their health status on a regular basis in order to reinforce scientific research on ILI surveillance practices. The total number of accounts amounts to 55.000. The GGM website contains all kind of education material including digital lessons on influenza, epidemiology and statistics, 'flu' games, et. al. for age groups from 6 to 18 years. Journalists, policy makers and researchers will find the latest ILI surveillance data. Over 135 publications and radio/tv items were dedicated to the GGM. This publicity was the main source of recruiting thousands of participants. Due to this success, the GGM team was encouraged to organize surveys in subsequent seasons. In the Netherlands, the project is officially acknowledged as a new, representative and scientifically reliable method of ILI surveillance (as confirmed in two studies) to be continued in the following years in tight cooperation with the Dutch health care authorities, represented by RIVM. We expect the federal health care authorities in Belgium to follow soon. In 2005, Sander van Noort introduced the GGM as www.gripenet.pt in Portugal where it currently attracts 3.800 Portuguese volunteers. In 2007, ISI in Italy introduced www.influweb.it.
Role in the proposal: We are team leader of WP 5. It is our task to introduce the internet-based monitoring system (IMS) in five European countries. In tight co-operation with our colleagues we look forward to launching national GGM-like systems, including database design and implementation, organisation, PR activities, translation of documents, etc. It is our responsibility to guarantee smooth coordination and effective implementation of all tasks in WP5.
AIBV team: Carl Koppeschaar, Sander van Noort and Ronald Smallenburg

Mr **Ronald Smallenburg**, director of Acquisto Inter BV (AIBV), Amsterdam: senior consultant in science communication and initiator of the first Internet-based Monitoring System (IMS) on influenza, the Great Influenza Survey or www.degrotegriepmeting.nl in the Netherlands and Belgium in 2003. Ronald is a senior consultant and manager of a range of science communication & research projects such as Project Kennislink, a Dutch language website and database with popular scientific knowledge on behalf of the Dutch Ministry of Education, www.kennislink.nl, www.gezondetenenbewegen.nl (Great Obesitas Survey) and will start a project on neuro-sciences next year.

Responsibilities: general management of AIBV; In EPIWORK: member of project steering committee and WP5 general coordinator, responsible for the overall coordination and administration of WP5.

Mr **Carl Egon Koppeschaar**, chief editor and initiator of the Great Influenza Survey, chief editor of www.kennislink.nl and science consultant, has extensive experience in the field having initiated various projects such as Kennislink and Great Influenza Survey. Other examples of interactive science communication projects on the internet are: www.gezondetenenbewegen.nl, which will focus on obesity and the necessity of a healthy life style; www.rekenmeemetabc.nl and ABC@home: a Dutch language website for students and the general audience to popularise mathematics.

Responsibilities: Carl is a free lance journalist and associate of AIBV. In EPIWORK: WP5 senior researcher and editor of the IMS.

Mr. **Sander van Noort**, researcher, mathematician and modeller. Together with three colleagues, sander designed and developed the scientific infrastructure of the Dutch/Belgian IMS, the Great Influenza Survey in 2003. Sander is currently working in Portugal at the Gulbenkian Institute (partner in EPIWORK) on his PhD, aiming to finish his thesis at the end of 2008. In 2005, Sander van Noort introduced the GIS as www.gripenet.pt in Portugal.

Responsibilities: Sander is an associate of AIBV. In EPIWORK: WP5 researcher and mode

Most significant publications:
Marquet R.L., Bartelds, A.I.M., van Noort S.P., Koppeschaar C.E., Paget J., Schellevis F.G., van der Zee J. 2006 An internet based monitoring of influenza-like illness (ILI) in the general population of the Netherlands during the 2003-2004 influenza season. www.biomedcentral.com/1471-2458/6/242.
Sander Paul van Noort (MSc), Marion Muehlen (MD, PhD), Helena Rebelo Andrade (PhD), Carl Koppeschaar (MSc), José Miguel Lima Lourenço (MSc), Maria Gabriela Miranda Gomes (PhD), Internet-based surveillance of influenza like illness (ILI) performs uniformly in the Netherlands, Belgium and Portugal. *Eurosurveillance*, *Volume 12, Issue 7-8, July/August, 2007*
www.eurosurveillance.org/em/v12n07/1207-223.asp.

6. London School of Hygiene and Tropical Medicine, UK

Team Leader: John Edmunds, London School of Hygiene and Tropical Medicine
Web page: www.lshtm.ac.uk
The London School of Hygiene & Tropical Medicine is Britain's national school of public health. Part of the University of London, the London School is an internationally recognized centre of excellence in public health, international health and tropical medicine with a remarkable depth and breadth of expertise. It is one of the highest-rated research institutions in the UK. Mathematical modelling has a long history at the London School (e.g. Ross and MacDonald's archetypal model of malaria, and Paul Fine's classic work on measles and pertussis), and the newly created Centre for the Mathematical Modelling of Infectious Diseases, at the School aims to build on this history, bringing together mathematical modellers across the different departments at the School. Prof. John Edmunds has recently joined the School from the Health Protection Agency to lead on this. Prof. Edmunds has a significant track record in the development and application of mathematical models to predict the spread of infectious disease and the impact of control programmes. He is a member of the UK Governments advisory committee on Pandemic Influenza (SPI), the SPI Modelling subgroup, as well as a number of other advisory bodies both nationally and internationally (e.g. WHO and ECDC). He has been at the forefront of developing novel techniques for elucidating contemporary mixing patterns. He co-ordinates the EU funded project POLYMOD that has the aim of improving mathematical models of the spread of infectious diseases through the collection, and analysis of contemporary mixing pattern data. Prof. Edmunds maintains close links with the HPA. He works collaboratively with the HPA on many projects, shares PhD studentships with the HPA and has an honorary appointment at the HPA. He also maintains close links with the Department of Health, and continues to advise them on pandemic influenza and other infectious disease control issues. His role on these committees will ensure that the results of EPIWORK will be disseminated to and exploited byrelevant bodies within the UK, and will help shape future policy.

Dr. Ken Eames is a post-doc at Cambridge University who will collaborate on the project with an active role in WP1. His research experience is in the development of models of disease spread through human mixing networks. Dr. Eames has worked on social mixing data collection projects, including current work on a Wellcome Trust funded public engagement project in collaboration with schools around the UK to design and carry out a research project to collect social mixing data.
Role in the proposal
LSHTM will contribute to the modelling of contact networks in WP1, designing approaches that provide accurate approximations to epidemic processes whilst being parameterisable with available data. LSHTM will also contribute to WP5 in the set up and deployment of the Internet-based monitoring system (IMS) in the UK. LSHTM team will also focus on extending the system to gather enhanced surveillance and behavioural data for the parameterisation of mathematical models.

LSHTM team: John Edmunds, Ken Eames.

Most significant publications

Cooper BS, Pitman RJ, Edmunds WJ, Gay NJ. Delaying the international spread of pandemic influenza. PLoS Med. 2006 Jun;3(6):e212. Epub 2006 May 2.

Pitman RJ, Cooper BS, Trotter CL, Gay NJ, Edmunds WJ. Entry screening for severe acute respiratory syndrome (SARS) or influenza: policy evaluation. BMJ. 2005 Nov 26;331(7527):1242-3.

J.M. Read,K.T.D. Eames, W.J. Edmunds, Dynamic social networks and the implications for the spread of infectious disease. *J. R. Soc. Interface*DOI: 10.1098/rsif.2008.0013(2008).

K.T.D. Eames, Modelling disease spread through random and regular contacts in clustered populations. *Theor. Popul. Biol*.73, 104-111 (2008).

K.T.D. Eames, M.J. Keeling, Coexistence and specialisation of disease strains on contact networks. *Am. Nat*.168, 230-241 (2006).

7. SMI - The Swedish Institute for Infectious Disease Control (SMI), Stockholm, Sweden

Team leader: Professor Olof Nyrén MD DMSci, SMI and MEB, Karolinska Institutet

Web page: www.smittskyddsinstitutet.se

SMI is a government expert agency, located on the Karolinska Institutet campus and having the following tasks:

- *Surveillance of notifiable infectious diseases according to Swedish law;*
- *Surveillance of the Swedish paediatric vaccination programme*;
- *Surveillance of the annual influenza vaccination of risk groups*;
- *National reference laboratory*;
- *Microbiological preparedness centre*;
- *Research institute*.

SMI collaborates with several government authorities and other organisations within the field of infectious disease control and prevention. SMI coordinates the Basic Surveillance Network (BSN), funded by the European Commission. Therefore, SMI has acquired considerable expertise in infectious disease surveillance, notably strengths and weaknesses of various methodological approaches. SMI is, further, deeply involved in the planning of responses to public health emergencies, among them pandemic influenza. Moreover, SMI combines epidemiological insight, specific expertise in virtually all communicable diseases, state-of-the-art laboratory facilities, and frontline basic research in virology and microbiology. In addition, there is an active group working with epidemic modelling, involved in the MODELREL and INFTRANS collaborations, and which takes advantage of the rich availability of detailed Swedish register data for microsimulation models.

The researchers at SMI are academically affiliated with Karolinska Institutet (KI), which is Sweden's only university especially focusing on biomedical sciences. Within Sweden, KI is responsible for some 40% of all medical research in universities and colleges and for about 12% of research education. There are more than 600 research units in some 30 departments, comprising approximately 2700 research staff and about 2500 postgraduate students. Researchers at KI publish annually more than 3000 papers, which receive 45% more citations than the world average.

More specifically, the epidemiologists are affiliated with the Department of Medical Epidemiology and Biostatistics (MEB), which is one of the largest and most successful units of epidemiological research in Europe. The department has extensive experience from large-scale population-based epidemiological research using various designs and has gathered considerable experience in Internet-based epidemiological research.

MEB has a mixed computer environment based on more than 30 UNIX/Linux and Windows servers. The department has a Storage Area Network (SAN) with 3.5 TB of raw disk, which can easily be expanded to 32 TB of raw disk. Of the total staff of close to 200, there are 16 full professors of epidemiology, more than 20 biostatisticians (3 full professors, 3 lecturers) and programmers with extensive experience of epidemiologic studies.

SMI role in the proposal The competence in epidemiological and biostatistical theory, experience in intricate large-scale field work, expertise in infectious disease surveillance, and the resources for

accommodating large and complex databases make SMI/MEB a suitable partner in WP6, where innovative approaches to infectious disease surveillance will be developed and evaluated.
SMI team: O Nyrén, A Linde, F Liljeros, L Brouwers, A Hulth, S Kühlmann, M Camitz, H Merk, P Saretok, JE Litton, C Bexelius, S Sandin.

Key personnel at SMI
Olof Nyrén, MD, PhD, Professor of Clinical Epidemiology at Karolinska Instiutet. Project leader at SMI. He will lead the work during the planning phase, oversee the field work, participate in the analysis work and report writing. He will also be the main contact person in the interaction with the different work-packages and centres within the EPIWORK consortium. He has considerable experience in conducting large-scale epidemiological investigations.

Annika Linde, MD, PhD, The Swedish State Epidemiologist. She is also a former professor of virology. She will participate in the planning, take an active part in the steering group that administers the field work, and participate in the analysis work and report writing. She will contribute virological and general infectious disease competence.

Sharon Kühlmann-Berenzon, PhD, statistician. She will participate in the planning, take an active part in the steering group that administers the field work, lead the analysis work, and participate in the report writing. Her statistical expertise constitutes one of the cornerstones of the group.

Hanna Merk, MD. She has extensive experience in administration of population-based disease surveillance through her central role in previous pilot studies, and through her work with infectious disease epidemiology at SMI. She will participate in the planning, take an active part in the field work, participate actively in the analysis work, and take a leading role in the report writing. The present work will be part of her PhD thesis. She will be part-time salaried by the project.

Significant publications
Liljeros F, Edling CR, Amaral LA, Stanley HE, Aberg Y. The web of human sexual contacts. *Nature* 411, 907-8 (2001).
Fored CM, Ejerblad E, Lindblad P, Fryzek JP, Dickman PW, Signorello LB, Lipworth L, Elinder CG, Blot WJ, McLaughlin JK, Zack MM, *Nyrén O*. Acetaminophen, Aspirin, and Chronic Renal Failure. *New Engl J Med* 345, 1801-8 (2001).
Camitz M, Liljeros F. The effect of travel restrictions on the spread of a moderately contagious disease. *BMC Med* 4, 32 (2006).
Edgren G, Hjalgrim H, Reilly M, Tran T, Rostgaard K, Shanwell A, Titlestad K, Adami J, Wikman A, Jersild C, Gridley G, Wideroff L, *Nyrén O*, Melbye M. Risk of cancer following transfusion from donors with subclinical cancer: a retrospective cohort study. *Lancet* 369, 1724-30 (2007).
de Blasio BF, Svensson A, Liljeros F. Preferential attachment in sexual networks. *Proc Natl Acad Sci U S A*. 104, 10762-7 (2007).

8. KULeuven - Katholieke Universiteit Leuven, Rega Institute for Medical Research, Belgium

Team Leader: Prof. Marc Van Ranst
Web Page: www.virology.be
Founded in 1425, K.U.Leuven is a Flemish University of Catholic signature with an international orientation. It has the legal statute of private institution. It transfers knowledge through high-quality interdisciplinary teaching. Its programmes integrate professional training into a broad ethical, cultural, and social context of education. Rather than passing on mere factual knowledge, it promotes the skills of identifying, formulating, and solving problems. It creates the necessary conditions for a stimulating educational experience. Special attention is paid to the steady evaluation of its teaching to enhance the student's capacity for independent study, to provide intensive individual guidance and an adequate evaluation system, to ensure high didactic qualities of the teaching staff, and to stimulate the use of new teaching methods and technologies.
The laboratory of Clinical Virology is part of the Rega Institute for Medical Research. This institution is an interfacultary biomedical research institute that is part of the K.U.Leuven, consisting of departments of

medicine and pharmacology. The laboratory of Clinical Virology is specialised in the molecular evolution of viruses like papillomaviruses, rotaviruses, RSV, hepatitis B viruses, hepatitis C viruses, coronaviruses and influenza viruses. In relation to viral evolution, we study the epidemiological spread of viruses in Belgium and Europe and this based on sample screening, questionnaires and data mining. Moreover, virus diagnosis and identification, together with the development of sequence-independent techniques for virus discovery and diagnosis form an important part of our research work.
Role in the proposal: We will have an active role in the WP5 in close collaboration with AIBV. It is our task to develop and apply standardized approaches for uniform surveillance of influenza-like illnesses (ILI) across European countries. It is our task to enhance the portability of the ILI surveillance system and the further refining of the ILI system in Belgium.
KULeuven Team: Prof. Marc Van Ranst, Dr. Piet Maes, Elke Wollants.

Key personnel at KULeuven:

Prof. Dr. Marc Van Ranst is full professor in Virology and Epidemiology at the University of Leuven Medical School, and the head of the Laboratory of Clinical Virology at the University of Leuven. He teaches Epidemiology and Virology at the University of Leuven, and also teaches Bioinformatics at Charles University in Prague in the Czech Republic. He was appointed in 2007 by the Belgian government as Interministerial Commissary for influenza pandemic preparedness planning.

Dr. Piet Maes is a senior postdoctoral researcher in the Laboratory of Virology at the Rega Insitute for Medical Research of the University of Leuven. Dr. Maes has extensive experience in zoonotic infections, bioinformatics, and modelling.

Most significant publications:
Matthijnssens J, Rahman M, Van Ranst M. Loop model: mechanism to explain partial gene duplications in segmented dsRNA viruses. Biochem Biophys Res Commun. 2006 3; 340(1):140-4.
Matthijnssens J, Ciarlet M, Heiman E, Arijs I, Delbeke T, McDonald SM, Palombo EA, Iturriza-Gómara M, Maes P, Patton JT, Rahman M, Van Ranst M. Full genome-based classification of rotaviruses reveals a common origin between human Wa-Like and porcine rotavirus strains and human DS-1-like and bovine rotavirus strains. J Virol. 2008; 82(7):3204-19.
Zlateva KT, Vijgen L, Dekeersmaeker N, Naranjo C, Van Ranst M. Subgroup prevalence and genotype circulation patterns of human respiratory syncytial virus in Belgium during ten successive epidemic seasons. J Clin Microbiol. 2007; 45(9):3022-30.
Van Ranst M. Chandipura virus: an emerging human pathogen? Lancet. 2004; 364(9437):821-2.
Clement J, Neild G, Hinrichsen SL, Crescente JA, Van Ranst M. Urban leptospirosis versus urban hantavirus infection in Brazil. Lancet. 1999; 354(9194):2003-4.

9. BIU- Bar Ilan University, Minerva Centre of Mesoscopics, Fractals and Neural Networks, Department of Physics, Israel

Team Leader: Shlomo Havlin
The MINERVA Centre for the Physics of Mesoscopics, Fractals and Neural networks headed by Shlomo Havlin was established in 1995 and is part of the Department of Physics at Bar-Ilan University. One of the main research activities of the Centre are studies of dynamical processes and complex systems using fractal and synchronization methods. In particular, the Centre had fundamental contributions to the analysis of physiological, ecological and climate signals as well as in developing methods that lead to better understanding of complex networks. The Centre has a fruitful collaboration since many years with the Institute for Theoretische Physik III (University Giessen) and collaboration with the Department of Pneumology of the Hospital of the Philipps-University in Marburg in 1998.
BIU Team: Prof **Shlomo Havlin** is the Director of the MINERVA Centre for the Physics of Mesoscopics, Fractals and Neural networks at Bar-Ilan University. Prof. Havlin received his PhD at Bar-Ilan University in 1972 with highest distinction. Since 1984, he is a full Professor of physics at Bar-Ilan University accompanied by several visiting Professor positions in Edinburgh, NIH (Bethesda) and Boston. Prof. Havlin is the former President of the Israel Physical Society (1996-1999) and, since 1996, an Elected Fellow of the

American Physical Society. Shlomo Havlin was awarded many national and international academic prizes. For example, the Landau-Prize for Outstanding Research (1988) and the Alexander-von-Humboldt Award (1992) and Nicholson American Physical Society Medal (2006). Prof. Havlin and collaborators developed the DFA method which is currently used in hundreds of studies of dynamical systems. His research interests are very broad and cover fields like statistical mechanics, phase transitions, percolation, optimization, diffusion in random systems, statistical properties of polymer chains, physics of disordered systems and fractals, chemical reactions, medical physics, statistical physics of biological and medical systems, granular media, traffic flow, atmospheric physics and econophysics. Prof. Havlin is author or coauthor of more 550 articles published in prestigious scientific journals like NATURE and Physical Review Letters, he is author and editor of 11 books and organized 10 international conferences in the last decade**. Dr. Reuven Cohen** received his PhD at Bar-Ilan University in 2003 with highest honours and now an Senior Lecturer in Mathematics at Bar-Ilan University. Dr. Cohen is a well-known expert in Complex Networks, is frequently invited to talks on international conferences. Reuven Cohen got several fellowships and awards, for instance, a Fulbright postdoctoral fellowship in 2004 and the AKSOE Socio- and Econo-physics young scientist award of the German Physical Society in 2005. His research focuses on resilience, percolation and topology of Complex Networks and he is the author of many well-cited articles about these subjects in Phys. Rev. Lett.

Most significant publications:

E Lopez, R. Parshani, R. Cohen, S. Carmi and S. Havlin, Limited Path Percolation on Complex Networks, *Phys. Rev. Lett*. 99, 188701 (2007).

L. Gallos, F. Liljeros, P. Argyrakis, A. Bunde, and S. Havlin, Improving Immunization Strategies, *Phys. Rev. E* 75, 045104 (2007).

N. Madar, T. Kalisky, R. Cohen, D. ben-Avraham, and S. Havlin, Immunization and epidemic dynamics in complex networks, *Eur. Phys. J. B* 38, 269 (2004).

R. Cohen, S. Havlin and D. ben-Avraham, Efficient Immunization Strategies for Computer Networks and Populations , *Phys. Rev. Lett.* 91 247901 (2003).

L. Muchnik , R. Itschak , S. Solomon and Y. Louzoun, Self-emergence of knowledge trees: Extraction of the Wikipedia hierarchies, *Phys. Rev. E* 76, 016106 (2007).

10. FBK –Fondazione Bruno Kessler, Italy

Team Leader: Stefano Merler, Fondazione Bruno Kessler, Italy.

Web page: http://mpba.fbk.eu/

The Fondazione Bruno Kessler (FBK) is a non-profit body with a public interest mission having private-law status and inheriting the history of Istituto Trentino di Cultura (ITC-created 1962 by the Autonomous Province of Trento). The total budget is currently about 34 M Euro yearly. FBK is the Centre for Scientific and Technological Research, a point of reference in the international scientific community and a hub for the development of technologies and applications with social and economical impact. The Center's applied and basic research activities aimed at resolving real-world problems and transferring technology to companies and public entities, also by founding 11 spinoff companies. The research staff at FBK consists of about 80 people on a permanent basis, and about 150 people on soft money. Half of FBK direct costs are covered by industrial contracts and European and National contracts. A substantial portion of FBK activities is in information technology. Other areas of activity are microsystems and applied physic. So far over 70 European contracts have been carried on by FBK in many successful Third, Fourth, Fifth and Sixth Framework projects, in some case with the role of coordinating partner.

Role in the proposal: Agent based models, geospatial technologies, statistical machine learning, bioinformatics and Grid computing are the main research aims of the Predictive Models for Environmental and Biological Data (MPBA) Research Unit, in this consortium. The group has undertaken modelling studies on infectious diseases, focusing on the development of agent based models for the spatio-temporal spread of pandemic influenza in Italy and the evaluation of intervention options. FBK will actively participate in WP2 and WP3 contributing with skills in developing and analyzing large-scale agent based models, embedded in a modular software environment (C/Python) through the use of databases, GIS and scientific visualization (VTK). Dr. Stefano Merler is FBK Senior Researcher. He has contributed to research in epidemiology, machine learning, geoinformatics and bioinformatics with applications to environmental risk analysis, landscape epidemiology and modelling pandemic outbreak scenarios. Dr. Cesare Furlanello is a FBK Senior Researcher and leader of the MPBA Project, since 1995. His main research interests are in the applications

of machine learning methods to medical and environmental data. He is an expert of computational statistics methods and predictive models for spatial data. Dr. Giuseppe Jurman is involved in the study of various mathematical aspects of machine learning and bioinformatics, with interest also in IT aspects of database structure and management. Marco Ajelli has contributed to research in epidemiology, focusing on the development of both agent based and compartmental models. S. Merler and M. Ajelli will be involved in the design and analysis of agent agent based models, in the case study analysis and will contribute to the development and analysis of agent based simulations in multi-scale systems. G. Jurman and C. Furlanello will contribute to the software implementation of the models and to the development of specialized data visualization techniques.

FBK team: M. Ajelli, C. Furlanello, G. Jurman, S. Merler

Most significant publications:

Marta Luisa Ciofi degli Atti, Stefano Merler, Caterina Rizzo, Marco Ajelli, Marco Massari, Piero Manfredi, Cesare Furlanello, Gianpaolo Scalia Tomba, Mimmo Iannelli. Mitigation measures for pandemic influenza in Italy: an individual based model considering different scenarios. PLoS ONE 3(3): e1790, 2008.

Marco Ajelli, Stefano Merler. The Impact of the Unstructured Contacts Component in Influenza Pandemic Modeling . PLoS ONE 3(1): e1519, 2008.

Marco Ajelli, Mimmo Iannelli, Piero Manfredi, Marta Luisa Ciofi degli Atti. Basic mathematical models for the temporal dynamics of HAV in medium-endemicity Italian areas. Vaccine 26(13): 1697-1707, 2008.

11. CREATE-NET -Center for REsearch And Telecommunication Experimentation for NETworked communities

Team Leader: Daniele Miorandi, Pervasive Computing & Communication Environments Area

Web page: http://www.create-net.org; http://www.create-net.org/pervasive; http://www.create-net.org/~dmiorandi

CREATE-NET is a research center established in 2003 in Trento Italy. The mission of the center is to convert talent and human capital into intellectual property and start ups for promoting European high-tech competitiveness. The institution is led by Prof. Imrich Chlamtac and pursues research and development activities in advanced communication and computing technologies. CREATE-NET supports its research activities through a Testbed based on an open environment principle, which provides distributed, operational, high-bandwidth telecommunications infrastructure for testing advanced technology and services. CREATE-NET works closely with governments, universities, SMEs, large companies and communities' worldwide alike, promoting European growth and exposing various layers of the global research world in Italy. In the frameworks of these collaborations CREATE-NET is involved in 12 European projects, 8 FP6-IST ones (3 as coordinator and 5 as partners) and 4 FP7-ICT ones. Funded projects by Italian Ministry of Foreign Affair and Research with leading institutions in the U.S., China and Israel have given CREATE-NET a respectable and competitive international name for itself. CREATE-NET is also a leader in fostering scientific community through the organization and sponsorship of various international events. Currently CREATE-NET is involved in more than 50 international conferences and workshops, in collaboration with IEEE, ACM, EU, ICST, IFIP and NSF. The 5 main Research Areas of CREATE-NET are: Pervasive, Security, Communication and Network Technologies, Multimedia Interaction and Smart Environment, OSCO (Open Distributed Systems for Communities and Business Organizations).

CREATE-NET will contribute to the EPIWORK project through the Pervasive Computing & Communication Environments team.

The Pervasive team, led by Dr. Daniele Miorandi, targets research in the field of pervasive computing and communications systems. The Pervasive team's activities and research focus on designing methodologies and tools for enabling pervasive networked devices to interface with the environment to support context-aware services. This includes design of architectures and protocols for large-scale heterogeneous networked systems, as well as algorithmic solutions for enhancing robustness and reliability in fully distributed and mobile systems.

Role in the proposal: The Pervasive team brings in the EPIWORK consortium skills and competences in the development of innovative non-intrusive data gathering solutions, based on the use of smartphones. In particular, two main contributions are foreseen, both within the framework of WP4 activities. First, to exploit the large availability of Bluetooth-enabled mobile phones to gather information on the contact patterns among people. Second, to provide an extension of Web-based interfaces for collecting data on people health

status, based on the use of mobile phones as target devices. CREATE-NET team will also contribute to the project's dissemination activities.

The team has experience in developing middleware platforms based on J2ME, specifically tailored to mobile phones (see, e.g, www.create-net.org/pervasive/u-hopper), as well as research competences on opportunistic communications. The Area Head, dr. Daniele Miorandi, is currently the coordinator of the BIONETS project (www.bionets.eu), funded by the EC in the framework of the FP6-FET Proactive Initiative on Situated and Autonomic Communications.

CREATE-NET team: D. Miorandi, I. Carreras.

Most significant publications:

I. Carreras, D.Tacconi, “U-Hopper: User-centric Heteogeneous Opportunistic Middleware”, in *Proc. of BIONETICS*, Budapest, Hungary, December 2007

I. Carreras, I. Chlamtac, F. De Pellegrini and D. Miorandi, “BIONETS: Bio-Inspired Networking for Pervasive Communication Environments”, *IEEE Trans. Veh. Tech.* , vol. 56, n. 1, pag. 218-229, Jan. 2007.

I. Carreras, D. Tacconi, D. Miorandi, “Data-Centric Information Dissemination in Opportunistic Environments”, in *Proc. of IEEE MASS*, Oct. 2007.

12. - FFCUL- Faculty of Sciences University of Lisbon

Team Leader: Mário J. Silva

Web Page: http://lasige.di.fc.ul.pt http://ptmat.ptmat.fc.ul.pt/

The Fundação da Faculdade de Ciências da Universidade de Lisboa (FFCUL) is a private non-profit organization, created in 1993, as an initiative of the Faculty of Sciences of the University of Lisbon. FFCUL acts as the front institution for a Portuguese scientific collaboration of multiple research groups, with more than 200 ongoing projects. Many of these R&D activities are developed together with international teams and are funded both at national and European levels. Its main purposes are to promote research and technological development activities, provide qualified human resources training and offer consulting expertise and knowledge dissemination. FFCUL has a large experience regarding EC project development, being responsible for the management of around 30 ongoing FP6 projects. Examples of important projects include Transfer, Nearest, Hidenets, Crutial, TargetScreen2, Sensoria, Watch, Esonet and EuroCareCF. FFCUL will administrate the participation of the Large-Scale Informatics Systems Laboratory (LASIGE) and Center for Mathematics and Fundamental Applications (CMAF). LASIGE is a research unit of the Department of Informatics with research lines in Biomedical Informatics, Communication System Software and Middleware, Fault and Intrusion Tolerance in Open Distributed Systems, Global Computing, Human Computer Interaction and Multimedia, Information Management, Timeliness and Adaptation in Dependable Systems. LASIGE has approximately 90 collaborators, 27 of which hold a doctoral degree. Within LASIGE, the XLDB Group and their researchers of the Biomedical Informatics research line will be directly involved in EPIwork. The group researches systems for data analyses, information integration and user access to large quantities of complex data from heterogeneous platforms. Current research activies span geographic information retrieval, text mining and natural language processing, web archiving and search, information visualisation, and biomedical informatics. Current EU-funded projects include CRUTIAL, GORDA and HIDENETS.

CMAF is part of the Complexo Interdisciplinar of Lisbon University (CIUL), which exists as a research infrastructure for more than 30 years, becoming part of the University of Lisbon in 1992. It is a modern facility dedicated exclusively to the support of research and post-graduate training.

Role in the project: The University of Lisbon will lead the development of the platform for mediating access to distributed collections of public health data. The platform will innovate by adopting web2.0 principles for sharing datasets, algorithms, visualizations, and other items relevant to the study of epidemics. The biomathematicians will work closely with TAU and FCG-IGC (participants no. 3 and 2 of this project, respectively). FFCUL will be responsible for WP3, and will participate in WP1 and WP4.

TEAM members: Mário J. Silva heads the XLDB Group of LASIGE. He has Ph.D. degree from the University of California, Berkeley, USA (1994). He joined the University of Lisbon in 1996, where he is now Associate Professor (with Habilitation) in the Department of Informatics. He has published over 70 refereed technical papers and book chapters. He leads a research team of over ten faculty, graduate students and technical staff at LASIGE on information integration and biomedical informatics (XLDB Group, http://xldb.fc.ul.pt). He has strong ties with industry in various roles, as staff, consultant, entrepeneur and

leader of a technology transfer unit at the university. **Nico Stollenwerk** heads the Biomathematic group at CMAF. He obtained his PhD from Aachen University respectively Clausthal University while working as researcher at the Research Center Juelich, all Germany, then as post doctorate researcher at Cambridge University and London University, both UK, recently at Gulbenkian Institute of Science and Lisbon University, Portugal. He has published more than 25 scientific contributions in international peer reviewed journals and refereed or invited scientific book contributions (journals like Science, Physica D, Journal of Theoretical Biology and Proceedings Natl. Acad. USA), mostly in the fields of epidemiological modelling and data analysis, parameter estimation and model validation, applied to e.g. pre-vaccination and post-vaccination measles, meningitis, dengue fever. **Fabrício Alves Barbosa da Silva** obtained a PhD (2000) from the University Pierre et Marie Curie (Paris VI) in parallel and distributed computing. He was a postdoctoral researcher and lecturer at University of California, Irvine, in 2001, and has been affiliated with several Brazilian Universities between 2001 and 2007. He is currently an Invited Assistant Professor at the University of Lisbon He presently coordinates the development of a epidemiologic surveillance system over a grid platform, which includes researchers from institutions such as University of São Paulo, UNIFESP and Mackenzie University. He has published over 40 refereed technical manuscripts. **Francisco M. Couto** obtained a PhD (2006) from the University of Lisbon in Bioinformatics. He was an invited researcher at CNRS, EBI and Bioalma during his PhD studies. He is currently an Assistant Professor at the University of Lisbon, Faculty of Sciences, where he coordinates the Master in Biomedical Informatics. He is currently a member of the LASIGE research group, coordinating the Biomedical Informatics research line. He received the Young Engineer Innovation Prize 2004 from the Portuguese Engineers Guild. Until March 2008, he published over 20 refereed manuscripts with more than 100 citations in total. **Frank M. Hilker** obtained a PhD (2005) from the University of Osnabrueck (Germany) in Applied Systems Science, which is an interdisciplinary programme combining mathematics, computer science, physics and modelling. He was a postdoctoral fellow in the Marie Curie Excellence Team in theoretical epidemiology at the Instituto Gulbenkian de Ciencia (Portugal) and is currently an Alberta Ingenuity Fellow at the Centre for Mathematical Biology at the University of Alberta (Canada). He will join CMAF with an independent research position in September 2008. His fields of research are in mathematical epidemiology and ecology. He has published 15 peer-reviewed papers in international journals (including Nature, American Naturalist, Physical Review E, Biological Invasions) and won a number of prestigious awards and fellowships (e.g., Alberta Ingenuity, Honourary Killam, Japan Society for the Promotion of Science, Konrad-Adenauer-Foundation). **Carlota Rebelo** is currently an Assistant Professor within the Mathematics Department of the University of Lisbon, Faculty of Sciences. Her research interests are focused on ordinary differential equations and applications to epidemiology. In the recent years she mantained a collaboration with Gabriela Gomes (IGC) in order to study theoretical aspects of mathematical models in epidemiology. She is also a member of CMAF (Centro de matematica e Aplicacoes Fundamentais).

Most significant publications:

Fabricio A. B. da Silva, Henrique Fabricio Gagliardi, Eduardo Gallo, Maria Antonia Madope, Virgílio Cavicchiolli Neto , Ivan Torres Pisa and Domingos Alves. IntegraEPI: a Grid-based Epidemic Surveillance System. Studies in Health Technology and Informatics, v. 126, p. 197-206, 2007.

Massad E, Chen M, Ma S, Struchiner CJ, Stollenwerk N, Aguiar M (2008) Scale-free network for a dengue epidemic. Applied Mathematics and Computation 159,376-381.

F. Couto, M. Silva, V. Lee, E. Dimmer, E. Camon, R. Apweiler, H. Kirsch, and D. Rebholz- Schuhmann. GOAnnotator: linking electronic protein GO annotation to evidence text. Journal of Biomedical Discovery and Collaboration, 2006.

Henrique F. Gagliardi, Fabrício A.B. da Silva, and Domingos Alves. Automata Network Simulator Applied to the Epidemiology of Urban Dengue Fever. Alexandrov et al. (Eds.): ICCS 2006, LNCS 3993, pp. 297 – 304, 2006.

Stollenwerk N, Martins J, Pinto A (2007) The phase transition lines in pair approximation for the basic reinfection model SIRI. Physics Letters A 371, 379-388.

Margheri, A., C. Rebelo, Some examples of persistence in epidemiological models, Journal of Mathematical Biology, 46, (2003), 564-570.

M.G. Gomes, A. Margheri, G. Medley, C. Rebelo, Dynamical behaviour of epidemiological models with suboptimal immunity and nonlinear incidence, Journal of Mathematical Biology, 51, (2005), 414-430.

Hilker FM, Langlais M, Malchow H (2008) The Allee effect and infectious diseases: extinction, multistability, and the (dis-)appearance of oscillations. American Naturalist, to appear.

B2.3 Consortium as a whole

The project description readily conveys the need for a wide variety of skills and competencies, ranging from complex systems theory and computational modelling to computer science, statistical physics and epidemiology. The consortium consists of 12 teams in 8 different countries that provide these competencies and that have skills and expertise that are documented by numerous publications and participation and leadership roles in previous European network projects. In the Diagram 3 we show the interaction network where each nodes represent the consortium teams and the links the dependency of work on each WP departing from the WP leader.

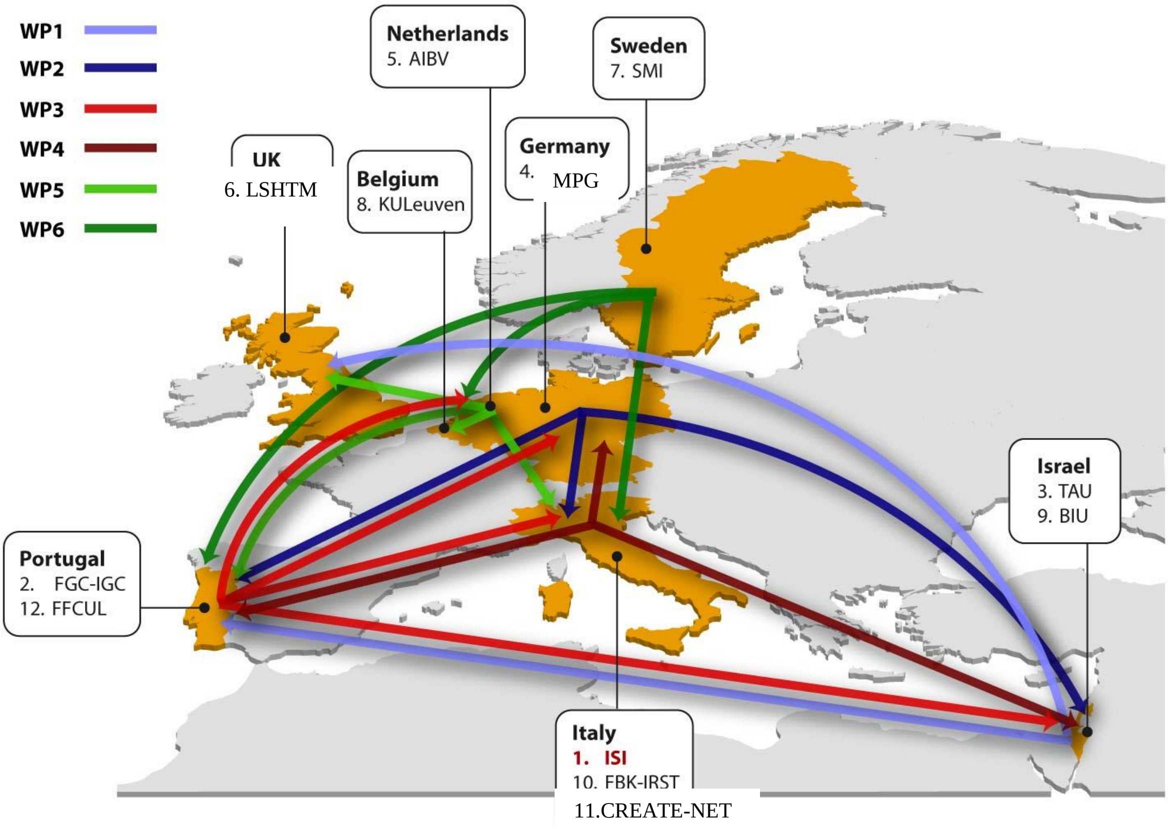

Diagram 4: Illustration of the Consortium

The map shows the partners of the Consortium and the collaborations envisioned by the project for each research work package. Arrows depart from the country of each WP leader.

The consortium represent a truly interdisciplinary effort listing epidemiology and public health (SMI, LSHTM, KULeuven) specialists, mathematical epidemiologists and biologists (FGC-IGC,TAU, FFCUL), computer scientists and information scientists (FFCUL, ISI), computational modellers (FBK,ISI, MPG) and physicists (BIU,MPG, ISI). The consortium includes also expert in the development of new networking technology (CREATE-NET) and a management firm (AIBV) with expertise in the deployment of infrastructure. Finally the social and behavioural expertise is guaranteed by the team working to pandemic preparation plans and exercise which are expert in the social/behavioural issues during major epidemics (KUL, SMI, LSHTM,TAU etc.). The SMI is including key researchers as prof. F.Liljeros who is a sociologists working on the social part related

to epidemic behaviour. As it is possible to see in Diagram 3, each WP has an active partner with epidemiological expertise. This is crucial in a project aiming at producing non-incremental results toward the development of a European epidemic forecast infrastructure. The consortium enlists also three teams (ISI, BIU, MPG) which are at the forefront of the research in complex systems. These teams have a crucial role with respect to the objective of the present call. The public health involvement (direct with partners SMI, KULeuven and indirect with contacts in the UK, Israel, ECDC, JRC, Portugal) in the project will eventually guarantee the exploitation and application of the project results in the epidemiological field. The specific expertise and a detailed list of the role of each team in the project is reported in Sec.2.2.

i) Sub-contracting:

As we do not have local coordination for introducing the IMS in France, Spain and Germany at the moment, we need to select these. The preparation for the database and website templates are done centrally and the subcontractors will deploy the IMS in the respective countries taking into account the specific mapping/representation solutions as well as finding the optimal granularity for the data acquisition and statistical sampling. This has to be devised in conformity with administrative divisions and historical records and consider the national mobility patterns. Communication and recruitment strategies will need to be devised to target the different populations of the 'new' IMS countries, each characterized by different habits (e.g. different diffusion of the Internet use in the population, different access to national media, different structures and organizations of school to contact for educational projects, etc.) and therefore reactions and feedbacks to the implemented strategies.Local coordination is also needed for weekly updates, PR and marketing activities for recruitment of volunteers, press presentation and communication, etc.

It is worth remarking that subcontractors have not to be considered member of the consortium and are not expected to provide strategic input concerning the goal and direction of the project. The subcontractors will just deploy the IMS according to the project requirements and will ensure the delivery of the data collection at the end of each year or in the database synchrony in the format specified by the consortium. The subcontractors are not scientific partners. They will not be part of any governing body of the project and will not participate to the scientific roadmap of the project. Their activities will be just restricted to the IMS deployment and no other collaborations are envisioned. The data resulting from subcontractors activities are just contributing to deliverable 5.3, 5.5, 5.7. More precisely the subcontractors are asked to deploy and operate the locally assigned IMS servers according to the specifics and directions of the consortium, to guarantee their operation and provide the consortium with the seasonal data gathered with the IMS. The data will be provided according to the format specified by the consortium.

Local IMS deployement requires expertise in ICT and medical and bioscience communication and is a part time job of an estimated 0,4 Full Time Employee on a year basis. In total, an additional 60 PMs in four years time are needed. We have identified suitable sub-contractors with the necessary expertise in the Robert Koch Institute in Germany, CG Essonne in France and Instituto de Salud Carlos III in Spain.

ii) Other countries:
DOES NOT APPLY

iii) Additional partners:
DOES NOT APPLY

B2.4 Resources to be committed

The principal resource required to carry out the project is personnel. In the following we provide the detailed description of the resources that each team will commit to the project.

ISI is committing 140 months of senior research staff effort and will hire: one post-doc for the entire duration of the project who will work on the development of the IMS in WP5; one post-doc for the last 3 years of the project who will work on the epidemic modelling platform of WP4; staff support staff for the entire duration of the project (48 months) to help with the administrative and coordination aspects of the project (36 months in WP7 and 12 months in WP8). The ISI research unit has a specific laboratory with a focus on computational epidemiology listing 6 senior researchers who will contribute to this project. The ISI team brings skills in the theoretical and computational modelling of large scale complex systems and networks. The ISI staff members are also expert in automated data mining and aggregation and computational tools that support professional knowledge management.

FGC-IGC seeks to hire 4 researchers, to work full time for the duration of the project: two postdocs that will work on WP1 and WP2, respectively; and two experienced researchers with the necessary competences of system engineering and science communication for WP5. The experienced researchers will be hired with stipend of 1500€, in accordance with the subsidies of the Portuguese Foundation for Science and Technology (FCT) plus Social Security benefits (1000€ per researcher per year).The IGC team will commit two senior researchers, a theoretical epidemiologist and a science communicator, that will contribute to the whole project and to WP5, respectively. This is, however, a conservative estimate. The IGC Theoretical Epidemiology Group at the IGC counts current with 20 members, all of which are expected to contribute indirectly to this project. Likewise, components of this project will synergise with the IGC Communication Office. The IGC has a well-established and structured in-house management and financial unit, is well-equipped with IT and communication support equipment, and will provide the underlying logistic and administrative support necessary to the project.

The **TAU** team intends to employ one senior research associate (with PhD), one postdoctoral fellow, and one PhD student. The senior researcher and postdoctoral fellow will be working on most aspects of Work Package 1. In particular, this will include the models of seasonality and predictions for recurrent epidemics, analysis of clustered contact networks and otherwise structured networks (see also WP2), and parameter estimations for modelling Israeli influenza data. The PhD student will be working on spatial modelling of influenza time-series data collected in Israel (WP1&4). All researchers will be working on immunization scenarios and their implications.

The **MPG** anticipates to commit 2x48 months of PhD-students to WP2. One student will work on the statistical analysis of human mobility networks, the analysis of proxy networks (eurobilltracker.com, bookcrossing.com and geocaching.com) and the development application of numerical techniques to identify the multi scale community structure of European countries. The second student will work on the design and analysis of mathematical and numerical methods to investigate the impact of metapopulation networks on the statistical properties of social contact

networks in the network-network duality focus of WP2. The team makes also available to the project its computational infrastructure to do high-performance computing consisting of several high performance clusters for a total of about 600 CPUs / 1700 cores with about 7TB of Memory.

AIBV (coordinator of WP5) will commit three senior staff people to this project. A total of 96 PMs of experience in science communication, senior project management and modelling will be dedicated to this project in four years. Two of the seniors will design, develop and implement a central IMS database for five 'new' IMS countries. We will also design, develop and manage an internet database with English language documents as part of one of the outcomes of WP 3. Furthermore, we will do the overall coordination of all the tasks involved with WP 5. Our post doc is a scientific researcher, modeler and chief designer. We will hire a project assistant for regular duties related to the coordinating the nine tasks of WP5 in five 'new' and four 'old' IMS countries. For assistance in design and development of the database infrastructure and internet database we will hire additional consultancy capacity on limited and short term basis. In summary the AIBV will use the asked resources to hire a senior research associate for a total of 24 MM, 16 MM of post Doc and fund 30MM of two AIBV senior investigators. AIBV will also provide 26 MM of own non-costed resources. Finally, as we do not have local coordination for introducing the IMS in France, Spain and Germany at the moment, we need to select these through subcontracting resources. Despite all preparation form database to website templates are done by us, local coordination is needed for weekly updates, PR and marketing activities for recruitment of volunteers, press presentation and communication, etc. Local coordination requires expertise in ICT and medical and bioscience communication and is a part time job of an estimated 0,4 FTE on a year basis.

The **LSHTM** team will contribute with 51 months to the project. The requested funds will allow the hiring of one post-doc for a period of 30 months and one post-doc for a period of 18 months. They will work on the modelling of contact networks in WP1 and on the deployment and set up of the Internet-based surveillance system (IMS) in the UK. Additional funds are requested to partially cover staff efforts and for travel costs associated.

The **SMI** team will lead the WP6.. The team will first work with the implementation and testing of the IMS (month 1-24), full-scale running of the IMS (month 12-36), launching of the PBA (month 6-24), full-scale running of the PBA (month 24-36), administration of the validation questionnaires for PBA (month 24-36), database development, as well as retrieval, verification and cleaning of data (month 6-48). The team request funds for a research coordinator and a PhD student will be half-time assigned to the projects on 50% of full time throughout its duration in order to exploit the scientific opportunities for a total of 72 MMs; together with the senior researchers at SMI they will design questionnaires, develop a plan for data analysis, carry out analyses of associations between social, behavioural and lifestyle-related determinants for infection, analyze the validation study, and utilize data in epidemic forecasting in collaboration with researchers from other collaborating centres within this project. In addition, SMI is committing 78 MMs of senior research staff.

The **KULeuven** team requests the funding of a half time senior researcher (24MMs) and will also commit 3 MMs of own costed resources. Data collected over the past years using the ILI surveillance system in the different participating countries, will be analysed to come to a set of

symptoms to define ‘influenza-like diseases’. This standardised list of symptoms will be confirmed by analysing samples of some selected volunteers from each participating country. The answers of these volunteers to the questionnaires will be scored in relation to clinical and laboratory findings. Samples taken from volunteers, found positive for influenza-like disease by the surveillance system, will be analysed for the presence of influenza virus and other respiratory viruses.

The **BIU** team intends to hire two researchers – one post doctoral researcher and one Ph.D. student for the work on EPIWORK – with a total of 80 PMs derived from the EC requested contribution, and 16 PMs from own non-costed resources Both researchers will be employed for the entire period of the project. The doctorate student will focus on the tasks related to WP3 and will work on empirical construction of network of disease spread and study of the dynamical and structural properties of the obtained network. Postdoctoral researcher will work on development of better immunization methods in contact methods (WP1) addressing both cases – when the network is not known and when it is known completely. Both researchers will work on WP2 constructing realistic models of networks embedded in space. This will require analysis of networks constructed from the empirical data for WP3 and application and further extension of the theoretical methods developed for WP1.

Funds requested by the **FBK** team will support staff efforts and travel costs for project meetings and workshops. More precisely, the asked resources will be used to hire a 3-year post-doctoral research position (36PMs) and to fund 8.5PMs of three senior investigators to service the necessary demands of the project for data integration, model design and development (WP2 and WP3).

The **CREATE-NET** team will contribute 38PMs to the EPIWORK project. Most of the resources will be used in WP5, where D. Miorandi, I. Carreras and a junior figure (to be hired) will be employed in order to carry out the activities foreseen in T5.7 and T5.8. Contributions will also be provided in the framework of the project dissemination activities (WP8). With respect to the latter, the deep involvement of **CREATE-NET** in conferences sponsorships and organization (more than 50 events in 2007) will be leveraged to enhance the project visibility on a global scale. In summary, the requested contribution will be used to fund 20PMs of a junior researcher and 18PMs of two senior researchers of the CREATE-NET team.

FFCUL is committing 51 months of senior research staff effort and will hire 1 doctoral and 1 full-time software engineer for 3 years each, and another doc/post-doc for 1/2 of the project duration. The post doc hired for 2 years will work on population models and contact networks. The doctoral student and software engineer will work full-time for 3 years, on the epidemic marketplace and its integration with the modelling platform. The participation of FFCUL involves two groups from the University of Lisbon: the staff members with expertise in medical informatics who will be responsible for the epidemic marketplace platform and its integration with the epidemic modelling platform, and the mathematicians who will research epidemic models.

B 3. Impact

B3.1 Expected impacts listed in the work programme

This proposal aims to bring about a paradigm shift in the epidemic forecast of infectious diseases. The goal is not simply to reproduce known features of the epidemic, but to forecast trends in its future evolution in order to help develop new strategies to ensure its containment/mitigation over the long term. The successful realisation of this ambitious goal requires a pan-European approach, bringing together partners with different fields of expertise (theoretical computational simulation and empirical data gathering) and combining the resources of existing measurement infrastructures. The proposed outcome, beyond being merely practical in nature, can have a clear impact in the theoretical application of complex systems theory to the study of large techno-social systems. The change of focus from reproducing data to forecasting trends will contribute to the development of new general classes of models aimed at quantitative prediction, open thus the possibility to new lines of research and place those in the proper framework to be adopted as a mainstream objective of ICT.

The project seeks a multidisciplinary research effort that, through computational thinking, promises a radical change in our forecast capacity and the development of computational approaches armed with predictive power in complex social systems. This is exactly one of the main objects of the new FP7-ICT program *Science of Complex Systems for Socially Intelligent IC.* In particular the present project, while pursuing its own research agenda, touches upon most of the focus point of the ICT program. Among others:

- Understanding the limit of predictability in systems in order to get faithful predictions in large scale complex systems.
- Development of computational methods that help to characterise the nature and impacts of effects that can occur as systems massively scale up.
- New protocols and experiments to gain realistic data on techno-social systems.
- The development of Data Rich probing technologies.

More in detail, the project has an impact both at the scientific, technological and social level. The consortium includes partners with a proven record of excellence in producing high impact scientific results published in scientific journals relevant to the areas covered by the project. We expect that the project will poise a solid and systematic scientific foundation for the development of a European epidemic forecast measurement and computational infrastructure. The teams involved in the project guarantee the necessary expertise to achieve consistent results that will be fruitfully disseminated to the scientific community at large.

The project is a truly interdisciplinary effort that is going to bridge different scientific communities and foster the interaction between complex systems science, ICT and epidemic modelling and data gathering. The impact of the interrelation between complex systems science and ICT goes beyond the specific research goals of the present project. The project aims at generating a successful example of the cooperation among these different approaches and perspectives tackling a concrete problem – predict the pattern and impact of infectious diseases- and showing the enormous

potential of the disciplinary cross fertilisation. On the one hand, complex systems science and modelling is used in a data driven perspective with the aim of producing quantitative results. On the other hand, the various scientific communities involved in the project will enlarge their set of concepts, tools and approaches by looking at the system from the new angle offered by taking into account the complexity of the systems and the necessary concepts needed to analyze those. It has to be noted as epidemic forecast cannot be obtained neglecting the systems' complexity, but at the same time this project provides a clear example where complex systems concepts are harnessed to obtain crucial predictive power. The main goal of the project implies major advances in the characterization, knowledge and modelling of large scale techno-social systems extending from the scale of the single individual to entire populations, providing the understanding and design of a new generation of tools and computational models that can support health policy makers in facing the long-term challenge posed by of infectious diseases.

Furthermore, the building of an epidemic modelling platform aimed that can be used outside the circle of practitioners and experts paves the way to a use of computing and simulation technology in policy making and forecast, enlarging the potential impact of complex systems science. The project wants to push forward the research agenda toward the deployment of a European epidemic forecast infrastructure. The final scientific impact of the project consists of producing major advances in enabling the creation of a computational platform that will allow fighting diseases in a completely new perspective. While the standard approach is the medical monitoring and intervention, we propose a novel perspective in which the integration of computational thinking, ICT technologies and systems' complexity will eventually lead in the next years to fight diseases by predicting their spread. Predictive power will allow focusing resources and intervention in advance where the disease is expected to strike, moving our intervention approach from passive (many times a-posteriori) to pre-emptive. This change of perspective is expected to have the same impact achieved by our capacity of predicting major meteorological events.

The proposed project in this phase is for a research infrastructure focussed on the macroscopic level of epidemic forecast and its implications for intervention planning. It carries, however, great potential to evolve into a data-model-computation framework capable of supporting a wider spectrum of biomedical research programmes connected to public health. Epidemiological models are also effective tools to formulate hypotheses concerning "microscopic" biological mechanisms that are consistent with their "macroscopic" epidemiological counterparts. These mechanisms can be tested in laboratories and contribute to the design of new medical interventions, such as vaccines or drugs. Ultimately, multi-level mathematical models can be developed maintaining an interface with both microscopic and macroscopic databases. Progressing towards increased novelty, we can envisage an extension of the infrastructure to complex diseases that are currently addressed by genetic epidemiology. However, these expansions are probably some 10 years into the future and, to ensure feasibility, the current proposal is restricted to epidemic forecast and intervention planning at the highest level.

Interdisciplinarity

This project offers a setting for intellectually stimulating exchange of experience and expertise between mathematical modellers, informatics scientists and engineers, medical epidemiologists and public health professional that, in cooperation, will devise an operational interface between data and

models providing excellent and equitable conditions for epidemiological modelling research in Europe. The potential contributions to the attractiveness of the European Research Area apply more widely to scientific performance, technological development capacity, policy-making and interaction with the society.

Society

The project has also a social impact. During the course of the proposed research activity, especially in the WPs concerning data sharing and gathering, the project will examine and develop tools and ICT technologies aimed at monitoring and surveillance of infectious diseases based on a novel collaborative approach. This has not an impact on ICT technologies but on the society at large. This would be one of the first large scale effort to use the social web to have large sample of the population collaborating on health monitoring issues by taking advantage of technology. This will amplify the public perception on the issue of communicable diseases and will set the bar for similar approaches in other health domains. The collaborative monitoring system will also act as a new media for information and risk awareness campaigns.

Policy making

This project will form the cornerstone of a consistent policymaking process informed by the integration of complex systems science in a socially-intelligent approach to disease forecast. A consequent impact will be improved preparedness, cooperation on required resources, logistic support and other associated processes in the context of infectious disease prevention and mitigation. The project will ease any further development in the area of infectious diseases epidemiology in Europe by the cross fertilization with computational thinking and complex systems science.

Education and training

Finally, we have to stress the impact of the project on the educational and human resource sides. Most of the resources requested to the European Commission are aimed at the hiring of postdoctoral scientists that will benefit of a truly interdisciplinary training. The wide spectrum of expertise represented within consortium will allow the graduate and post doctoral students to benefit from a level of exposure to different techniques and tools which would be hardly possible to achieve in any institutional disciplinary program.

B 3.2 Plan for the use and dissemination of the foreground

The consortium is aware of the importance of dissemination, collaboration and exploitation activities and it has planned a specific work package and deliverables in order to commit specific resources to this endeavour. In particular the project is devoting 4 to 5% of the total resources to dissemination, collaboration and exploitation, dividing equally among these three activities the allocated budget. The need for an intense dissemination, collaboration and exploitation effort is particularly acute in the interdisciplinary context of the present project that aims at involving physicists, computer scientists and epidemiologists. The projects results need to be communicated to diverse disciplinary areas bridging the language and methodological barriers. While the primary dissemination stream is surely represented by the scientific publications in high impact journals and

conference proceedings, the consortium aims at reaching the scientific community at large providing accessibility to the project main results through non technical papers and the media. Some specific lines of actions are:

- The consortium plans the writing of a project executive summary accessible to the non-specialist, avoiding technical language and mathematics as much as possible. Analogously, a final non-technical report summarizing the results achieved by the project will be provided at the end of the consortium activity.
- The consortium will set up a project web site that will work as a showcase of all the ongoing activities of the project and as a entrance point to the data and computational modelling platforms. By definition, the information platform and the epidemic modelling platform are aimed at involve the scientific community at large
- The consortium will organise a mid-term and an end of the project workshop aimed on the one hand at disseminating the project results to the community of scientists and on the other hand trying to involve and get feedback from external experts and researchers.
- The final workshop will be the occasion to compact the body of work carried out during the project and a specific publication in the form of a book is envisioned.

The projects information and modelling platform are inherently exploitation and dissemination tools. The data and algorithms available to the public on the platforms will be completely open and we aim at involving the community at large in their use. The two workshops will be used to have presentation tutorials and the consortium will engage all possible forms of scientific dissemination for these tools through appropriate software and technical communications on scientific journals. In addition, the platform will be tested at the member state level by providing them to the national or regional public health institutions and organising training sessions (software tutorials) on the usage of the platforms and critical interpretation of the results. These training sessions will be organized during the project workshops. As stated below a number of health institute and protection agencies will be engaged since the starting of the project and ad hoc software demonstration and training session will be organized with the various agencies involved or contacted in the project.

The project will make its best effort to engage with policymakers and government agencies to demonstrate the value and use of the project results, with a particular focus on the computational/data platform and the IMS system. This involvement will happen since the very start of the project. Indeed the consortium is in a very privileged position in this respect as we have access the policy making agencies of several countries such as Israel Center for Disease Control, the UK Health protection agency, the Swedish Institute for Disease Control, the Belgium federal Institute for Disease Control. These agencies are naturally involved in the project since the beginning with the presence of the teams' investigators who are also collaborating or with position in the agencies. In addition, we have already established contacts with the European center for disease control (ECDC) and the Joint Research Center of the EC. One representative from this institution will be seating in the advisory board of the project with the aim of monitoring the advances and tools generated in the consortium in order to readily design practical implementation of those in the agency policy making. The KUL and LSHTM are involved in European wide exercise for pandemic preparation and will allow a direct transmission of the consortium results in national preparation plans, if opportune. Finally the consortium is also in contact with European

joint research center in order to provide tools to their team devoted to population protection and intervention. Also in this case we are going to have one member of this institution seating in the external advisory board to facilitate the information sharing and communication.

The Internet based monitoring System (IMS) developed set up in the project is another extraordinary outreach opportunity. The IMS is conceived to inform and educate the population about the disease and to collect real-time information on the distribution of ILI through social collaborative web-services. The project aims at increasing the participation of large section of the population in the countries of the ISI, IGC and AIBV teams and to extend its implementation into five new countries. This corresponds to a vigorous outreach effort involving all media channels in order to reach the maximum number of people to be aware of the project. The IMS will be also a podium to advertise the EPIWORK project as well as an incredible outreach media for the results obtained during the course of the project.

The consortium is also committed to provide an effort toward joint activities in the FET framework. We will establish contact with other related IP and Strep project. We will consider having members of other projects to seat in the external advisory board also with role of liaison officer if strong connections can be found (for instance with project with disaster managements, social behaviour and policy making implications). We will explore avenues for collaborations and joint publications as well as act synergistically to mutually advertise projects' results on our public dissemination channels. The consortium will also ensure is presence and representation at FET initiatives and conference with talks and showcase exhibition, if possible. Finally the consortium is willing to be engaged in the definition of the FET roadmap toward the future research in the area.

All activities in the project will be continuously monitored with respect to the intellectual property and copyrights standpoints. In the risk of unethical behaviour or conflict with the national and international regulatory requirements, the project steering committee will quickly proceed on the appropriate corrective actions. This implies that all scientific papers will be written and published according to the international criteria concerning plagiarism, honesty of reference, etc. Furthermore, the project will endorse only works originating during the course of the project by authors involved in the project.
All mechanisms developed in the project are targeted to ensure that there is an open access to the data and models generated by the project to the scientific community at large. In this perspective the project promotes sharing of results and resources and open standards. There are four major sharing model types at work in this project:

- Software/algorithms sharing
- Data sharing
- Practice sharing —a description or paper to explain how to use a set of algorithms + parameters to analyze data
- Voting/recommendation mechanisms to promote access to the highly valuable efficient algorithms, datasets, and practices developed during the project.

All four components are equally important and are interlinked with each other. The project will work with Open Source Initiative (http://opensource.org) certified licenses, including but not limited to Apache License, 2.0, New BSD license, GNU General Public License (GPL), GNU Library or "Lesser" General Public License (LGPL), MIT license, Mozilla Public License 1.1

(MPL), Common Development and Distribution License, Common Public License 1.0, and Eclipse Public License. Finally, any Creative Commons license is acceptable.

B.4. Ethical Issues

All activities in the project will be continuously examined from the viewpoint of ethical issues and from the viewpoint of national and international regulations that might be applicable. Corrective actions will be taken as soon as there is a risk of unethical behavior or if the activities in the project do not fit with the national and international regulatory requirements.

Epiwork is mostly concerned with de-identified secondary data analysis. However it will collect health data with the IMS infrastructure. More precisely, Epiwork will support the upload, download and gathering of three types of resources such as:

1. Models and Algorithms.
2. Non-human subject research data, including data generated from models and algorithms (not obtained from living individuals), as well as data not obtained from living individuals or obtained from living individuals and professionally de-identified (including those from organizations such as the Census Bureau, the CDC and ECDC, World Health Organization (WHO), etc.)
3. Data obtained from the internet-based monitoring infrastructure and subject to privacy concerns. These data present concerns only in terms of the privacy of the IMI users.

In order to minimize risks to participants, data gathered with the IMS and made available to researchers will be prepared according to the following criteria: a) the identities of data subjects cannot be readily ascertained or otherwise associated with the data; b) the data identifiers removed and data properly anonimized; c) For the purpose of data analysis, the partners will only handle anonymous data or data in which the user cannot be identified; d) the project is committed to respecting the legislation with respect to privacy of information of citizens

The consortium will make sure that the IMS works in agreement with the different country laws in terms of privacy protection. The users of the IMS will be prompted to sign privacy agreement and informed consent as indicated by the various countries regulation. The consortium will make sure that the subsequent sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained. No databases with personal materials collected during the project will be sold under any pretext.

Last but not least, security is an ongoing endeavor. All servers of Epiwork will be set up to be scanned for external vulnerabilities constantly in order to continually evaluate our security posture and adjust as the situation requires.

ETHICAL ISSUES TABLE

	YES	PAGE
Informed Consent		
• Does the proposal involve children?		
• Does the proposal involve patients or persons not able to give consent?		
• Does the proposal involve adult healthy volunteers?		
• Does the proposal involve Human Genetic Material?		
• Does the proposal involve Human biological samples?		
• Does the proposal involve Human data collection?		
Research on Human embryo/foetus		
• Does the proposal involve Human Embryos?		
• Does the proposal involve Human Foetal Tissue / Cells?		
• Does the proposal involve Human Embryonic Stem Cells?		
Privacy		
• Does the proposal involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)	X	
• Does the proposal involve tracking the location or observation of people?	X	
Research on Animals		
• Does the proposal involve research on animals?		
• Are those animals transgenic small laboratory animals?		
• Are those animals transgenic farm animals?		
• Are those animals cloned farm animals?		
• Are those animals non-human primates?		
Research Involving Developing Countries		
• Use of local resources (genetic, animal, plant etc)		
• Impact on local community		
Dual Use		
• Research having direct military application		
• Research having the potential for terrorist abuse		
ICT Implants		
• Does the proposal involve clinical trials of ICT implants?		
I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL		